60862

Access DB# 111

4134

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: PATEL SUDHAKER Examiner #: 77018 Date: 2/22/02
Art Unit: 1624 Phone Number 30 84709 Serial Number: 09869668
Mail Box and Bldg/Room Location: CM1 4E17 Results Format Preferred (circle): PAPER DISK E-MAIL
4E12

If more than one search is submitted, please prioritize searches in order of need.

****

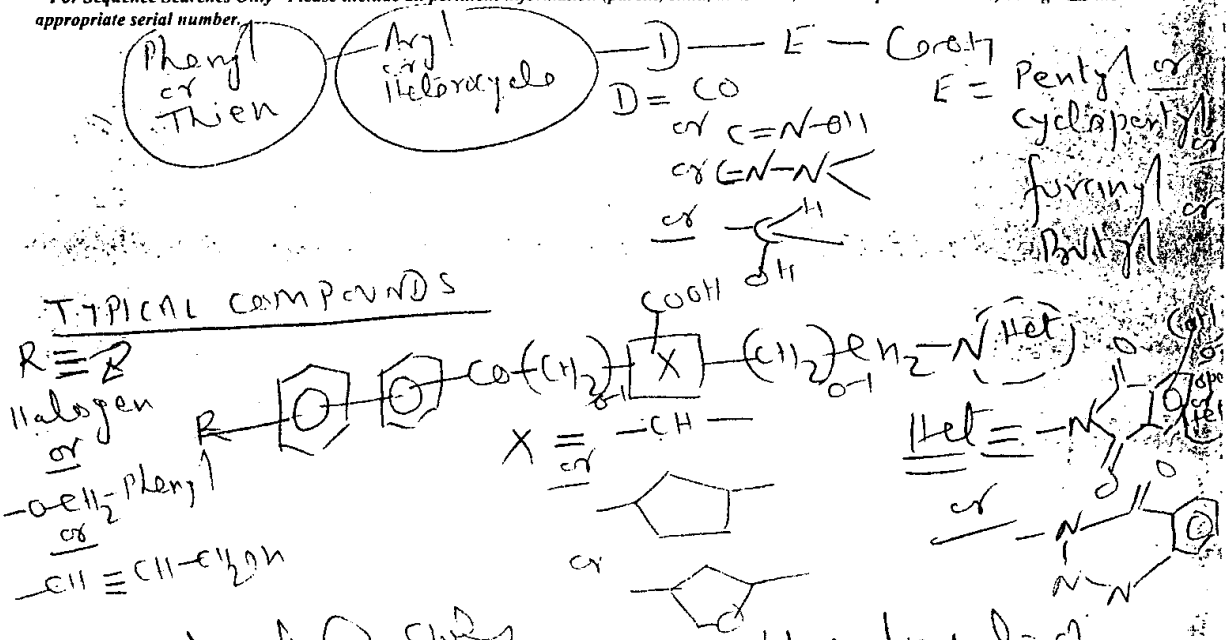
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims and abstract.

Title of Invention: USE OF SUBSTITUTED 4-BIARYLBUTYRIC & 5-BIARYLPENTANOIC ACID DERIVATIVES AS NITRIX METALLOPROTEASE INHIBITORS FOR THE TREATMENT OF RESPIRATORY DISEASES

Inventors (please provide full names):

Earliest Priority Filing Date: 12/30/1998

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



Need info @ cpds COMPOSITIONS & method of use/treatment of Asthma, ARDS, SILICOSIS, BRONCHITIS, copy of claims enclosed THX SBCB 1624

****

STAFF USE ONLY

Searcher: Paul Schulwitz
Searcher Phone #:
Searcher Location: 4B
Date Searcher Picked Up: 2/22
Date Completed: 2/25
Searcher Prep & Review Time: 90
Clerical Prep Time:
Online Time:

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#) 2
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN ✓
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

RECEIVED FEB 22 2002 TECH CENTER 1600/2900

POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 12C14 TEL. (703) 305-1954

PTO-1590 (8-01)

biphenyl case - Claim 2


```
=> d que
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L2              STR
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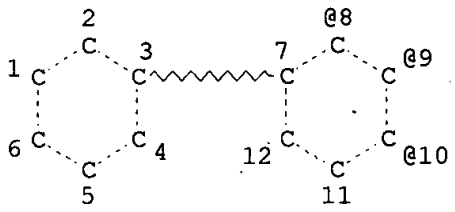

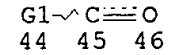


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  15

STEREO ATTRIBUTES: NONE
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L4  (       104)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(L)(MATRIX? OR METALLOPROTEA
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L5  (        35)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND RESPIR?
L6             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND L5
L8         69587 SEA FILE=REGISTRY SSS FUL L2
L9               STR
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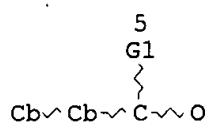
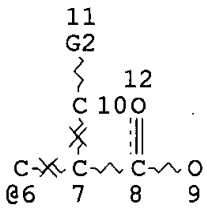
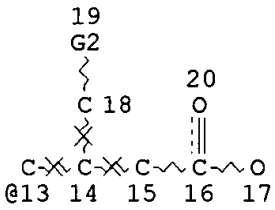
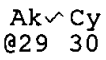
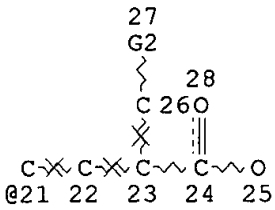
These results only contain one representative structure for each record. If you need to see more, let me know. None of these records appear to be about treating respiratory disease.











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VAR G2=CY/29
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CONNECT IS E1 RC AT 17
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DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 1
GGCAT IS MCY UNS AT 2
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E6 C AT 1
ECOUNT IS E6 C AT 2

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

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L12 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
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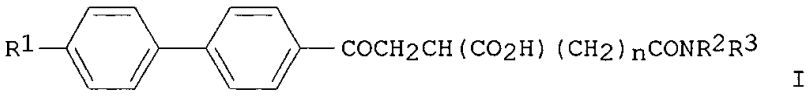
L15 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND ((RESPIR? OR BREATH? OR ASTHMA? OR BRONCH? OR LUNG?)/CT OR (RESPIR? OR BREATH? OR ASTHMA? OR BRONCH? OR LUNG?))

L14 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:816632 HCAPLUS
DN 135:357771
TI Preparation of biphenylbutyric acid derivatives as matrix metalloproteinase inhibitors
IN Park, Young-Jun; Ryu, Choon-Ho; Yoo, Ji-Uk; Chae, Myeong-Yun; Paek, Sang-Hyun; Kim, Kyung-Chul; Lee, Jeoung-Wook; Min, Hye-Kyung; Bae, Hae-Young; Oh, Eu-Gene
PA Samsung Electronics Co., Ltd., S. Korea
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001083445	A1	20011108	WO 2001-KR687	20010424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI KR 2000-21834 A 20000425
KR 2000-21835 A 20000425
OS MARPAT 135:357771
GI

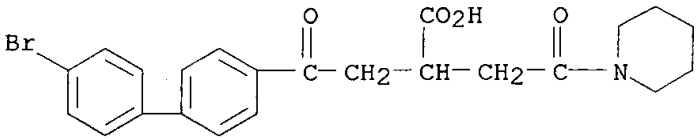


I

AB Biphenylbutyric acid derivs. I [R1 = H, alkyl, cycloalkyl, halo, cyano, etc.; R2, R3 = H, alkyl, aryl, arylalkyl, heteroaryl, cycloalkyl; n = 1, 2], inhibitors of matrix metalloproteinase, were prepd. E.g., 1,5-dioxo-1-(1-phenylcarbamoyl-1-ethylamino)-5-(4-bromobiphenyl-4-yl)-3,3-diethoxycarbonylpentane (prepn. given) was treated with NaOH to give 1,5-dioxo-1-(1-phenylcarbamoyl-1-ethylamino)-5-(4-bromobiphenyl-4-yl)-3-carboxylpentane (60%).

IT **372100-82-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylbutyric acid derivs. as matrix metalloproteinase inhibitors)

RN 372100-82-8 HCAPLUS
CN 1-Piperidinebutanoic acid, .alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



IT **372100-82-8P 372100-83-9P 372100-94-2P**
372101-05-8P 372101-06-9P 372101-07-0P
372101-10-5P 372101-11-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylbutyric acid derivs. as matrix metalloproteinase inhibitors)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:247168 HCAPLUS
DN 134:266035
TI Use of substituted 4-biarylbutyric and 5-biarylpentanoic acid derivatives for the treatment of multiple sclerosis
IN Fahrig, Thomas; Haning, Helmut; Riedl, Bernd; Braeunlich, Gabriele; Henning, Rolf
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001022951	A2	20010405	WO 2000-EP8890	20000912
WO 2001022951	A3	20011011		

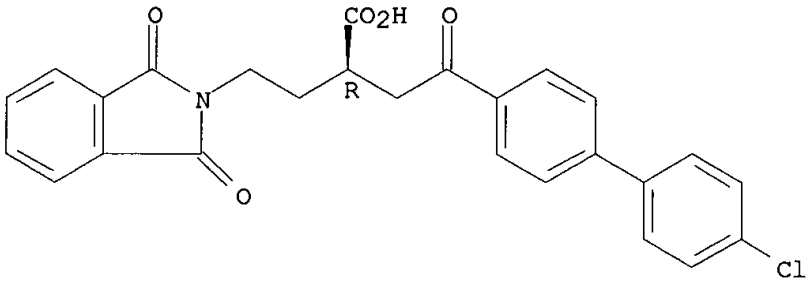
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1999-22710 A 19990924
OS MARPAT 134:266035
AB The title compds. (T)xA-B-D-E-CO2H [I, A = aryl, heteroaryl; B = aryl, heteroaryl, bond; each T is a substituent group; x = 0, 1, or 2; D = CO, CH(OH); E = two or three carbon chain bearing one to three substituent groups which are independent or are involved in ring formation], useful for the treatment of multiple sclerosis, were prepd. E.g., (rac)-2-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-4-(4'-ethoxy[1,1'-biphenyl]-4-yl)-4-oxobutanoic acid was prepd. Inhibitory activities of I against matrix metalloproteases was detd.
IT **179546-43-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(prepn. of 4-biarylbutyric and 5-biarylpentanoic acid derivs. for the treatment of multiple sclerosis)

RN 179546-43-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **179546-43-1P 179546-47-5P 179798-06-2P**
179798-07-3P 282095-17-4P 282095-19-6P
282095-22-1P 282095-24-3P 282095-26-5P
282095-29-8P 282095-31-2P 282095-34-5P
282095-36-7P 282095-38-9P 282095-40-3P
289485-12-7P 289485-13-8P 289485-14-9P
289485-16-1P 289485-17-2P 289485-18-3P
289485-20-7P 289485-21-8P 289485-22-9P
289485-25-2P 289485-26-3P 289485-27-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-biarylbutyric and 5-biarylpentanoic acid derivs. for the treatment of multiple sclerosis)

L14 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:608369 HCAPLUS
DN 133:193178
TI Preparation and use of substituted biaryloxo(oxobenzotriazinyl)alkanoates and related compounds for treatment and prevention of cerebral diseases.
IN Hinz, Volker; Haning, Helmut; Riedl, Bernd; Henning, Rolf; Stolle, Andreas; Keldenich, Jorg; Bruck, Antje; Schumacher, Joachim
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 60 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1031349	A1	20000830	EP 1999-103723	19990225
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2000050017	A2	20000831	WO 2000-EP1204	20000214
	WO 2000050017	A3	20010201		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,				

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1087761 A2 20010404 EP 2000-920435 20000214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI EP 1999-103723 A 19990225
WO 2000-EP1204 W 20000214

OS MARPAT 133:193178

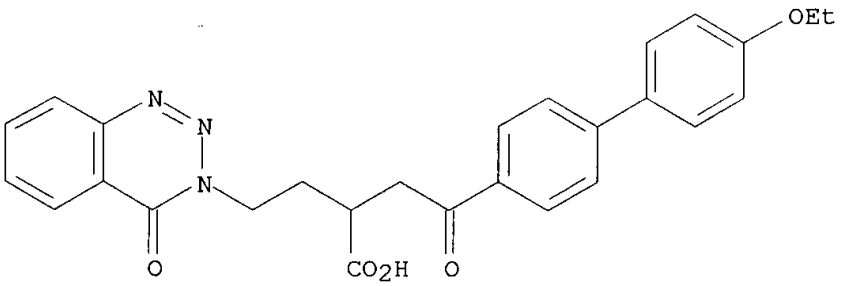
AB Use of TxABDECO2H [B = bond, (substituted) aryl, heteroaryl; T = F, Cl, Br, iodo, alkyl, haloalkyl, haloalkoxy, alkenyl, alkynyl, etc.; A = thienyl, furyl, pyrrolyl, thiazolyl, pyridazinyl, pyrimidinyl, Ph, etc.; x = 0, 1, 2; D = CO, CH(OH); E = chain of 2-3 C atoms bearing substituents R6; R6 = F, OH, alkyl, aryl, heteroarylaralkyl, alkenyl, etc.; pairs of R6 may form spiro or nonspiro rings; with provisos] for manufg. of drugs for the treatment and prevention of cerebral disease is claimed. Thus, 4-(4'-chlorobiphenyl-4-yl)-4-oxo-2-[2-(4-oxo-4H-benzo[d][1,2,3]triazin-3-yl)ethyl]butyricacid inhibited matrix metalloproteinase-1 and -2 with Ki = 2400 nM and 1.2 nM, resp.

IT **289485-13-8P**
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use of substituted biaryloxo(oxobenzotriazinyl)alkanoates and related compds. for treatment and prevention of cerebral diseases)

RN 289485-13-8 HCAPLUS

CN 1,2,3-Benzotriazine-3(4H)-butanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-4-oxo-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



IT **289485-13-8P 289485-14-9P 289485-17-2P**
289485-18-3P 289485-21-8P 289485-22-9P
289485-26-3P 289485-27-4P 289634-16-8P
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use of substituted biaryloxo(oxobenzotriazinyl)alkanoates and related compds. for treatment and prevention of cerebral diseases)

IT **199437-84-8**

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and use of substituted biaryloxo(oxobenzotriazinyl)alkanoates and related compds. for treatment and prevention of cerebral diseases)

IT **289485-09-2P 289485-10-5P 289485-12-7P**
289485-16-1P 289485-20-7P 289485-25-2P
289485-30-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use of substituted biaryloxo(oxobenzotriazinyl)alkanoates and related compds. for treatment and prevention of cerebral diseases)

IT **179546-47-5**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and use of substituted biaryloxo(oxobenzotriazinyl)alkanoates and related compds. for treatment and prevention of cerebral diseases)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

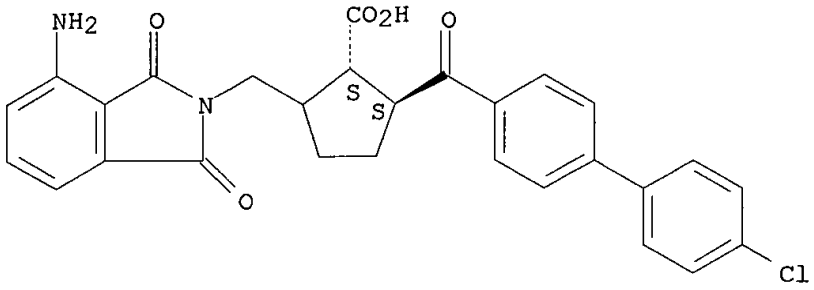
L14 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:439095 HCAPLUS
DN 133:219279
TI Evaluation of docking/scoring approaches: a comparative study based on MMP3 inhibitors
AU Ha, Sookhee; Andreani, Romana; Robbins, Arthur; Muegge, Ingo
CS Bayer Research Center, West Haven, CT, 06516, USA
SO J. Comput.-Aided Mol. Des. (2000), 14(5), 435-448
CODEN: JCADEQ; ISSN: 0920-654X
PB Kluwer Academic Publishers
DT Journal
LA English
AB An increasing no. of docking/scoring programs are available that use different sampling and scoring algorithms. A reliable scoring function is the crucial element of such approaches. Comparative studies are needed to evaluate their current capabilities. DOCK4 with force field and PMF scoring as well as FlexX were used to evaluate the predictive power of these docking/scoring approaches to identify the correct binding mode of 61 MMP-3 inhibitors in a crystal structure of stromelysin and also to rank them according to their different binding affinities. It was found that DOCK4/PMF scoring performs significantly better than FlexX and DOCK4/FF in both ranking ligands and predicting their binding modes. Most notably, DOCK4/PMF was the only scoring/docking approach that found a significant correlation between binding affinity and predicted score of the docked inhibitors. However, comparing only those cases where the correct binding mode was identified (scoring highest among sampled poses), FlexX showed the best fine tuning (lowest rmsd) in predicted binding modes. The results suggest that not so much the sampling procedure but rather the scoring function is the crucial element of a docking program.

IT **291298-43-6**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitor; comparative evaluation of docking/scoring approaches based on MMP3 inhibitors)

RN 291298-43-6 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4-amino-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-5-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-, (1R,5R)-rel-

(9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **291298-43-6 291298-44-7 291298-45-8**
291298-46-9 291298-47-0 291298-48-1
291298-51-6 291298-68-5 291298-78-7
291298-83-4 291298-84-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitor; comparative evaluation of docking/scoring approaches based on MMP3 inhibitors)
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:84604 HCAPLUS
DN 132:141951
TI Pharmaceutical compositions containing ACAT and MMP inhibitors for the treatment of atherosclerotic lesions
IN Bocan, Thomas Michael Andrew
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004892	A2	20000203	WO 1999-US13948	19990618
	WO 2000004892	A3	20000518		
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9947017	A1	20000214	AU 1999-47017	19990618
	BR 9912296	A	20010417	BR 1999-12296	19990618
	EP 1098662	A2	20010516	EP 1999-930483	19990618
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001000291	A	20010118	NO 2001-291	20010118
PRAI	US 1998-93639	P	19980721		

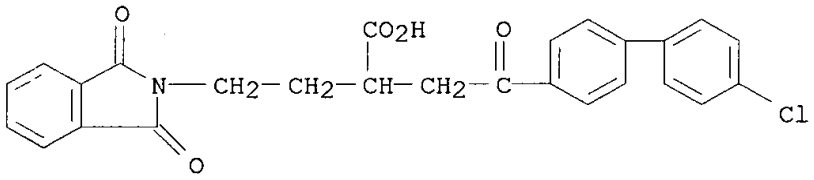
WO 1999-US13948 W 19990618

AB Acyl-CoA:cholesterol acyltransferase (ACAT) and matrix metalloproteinase (MMP) inhibitors are coadministered for the redn. of both the macrophage and smooth muscle cell component of atherosclerotic lesions, thus impairing the expansion of existing lesions and the development of new lesions and for the prevention of plaque rupture and the promotion of lesion regression in a mammal. The direct antiatherosclerotic potential of the combination of ACAT inhibitor, [[2,4,6-tris-(1-methyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl sulfamic acid, and the HMG-CoA reductase inhibitor, simavastatin, in rabbits was studied. A tablet contained 2-(4'-bromobiphenyl-4-sulfonylamino)-3-Me butyric acid 25 ACAT compd. lactose 50, corn starch 20, and magnesium stearate 5 mg.

IT **179546-41-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. ACAT and MMP inhibitors for treatment of atherosclerotic lesions)

RN 179546-41-9 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



IT **179546-41-9 179546-43-1**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. ACAT and MMP inhibitors for treatment of atherosclerotic lesions)

L14 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:670997 HCAPLUS

DN 131:283326

TI Matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics

IN Dixon, Brian R.; Chen, Jinshan

PA Bayer Corp., USA

SO U.S., 25 pp.
CODEN: USXXAM

DT Patent

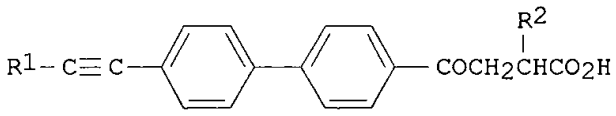
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5968795	A	19991019	US 1997-856694	19970515
PRAI	US 1996-645028	P	19960515		
	US 1996-70454	P	19960515		
	US 1996-70454	P	19960515		

OS MARPAT 131:283326

GI



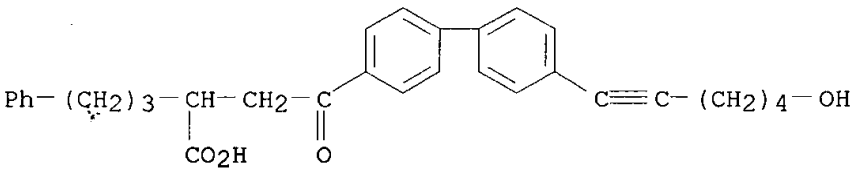
I

AB Matrix metalloprotease inhibiting compds., pharmaceutical compns. thereof and a method of disease treatment using such compds. are presented. The compds. are I (R1=CH2OH, (n-Pr)2NCH2, CH3CO2CH2, EtOCO2CH2, HO(CH2)2, CH3CO2(CH2)2, HO2C(CH2)2, OHC(CH2)3, HO(CH2)4, 3-HO-Ph, PhCH2OCH2; R2=3-phenylpropyl, N-phthalimidoethyl). These compds. are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophic epidermolysis bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, temporomandibular joint disease, demyelinating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plaque rupture. The present invention also provides pharmaceutical compns. and methods for treating such conditions.

IT **199672-16-7P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)

RN 199672-16-7 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, 4'-(6-hydroxy-1-hexynyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



IT **199672-16-7P 246177-93-5P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)

IT **179548-75-5P 179548-76-6P 199672-05-4P**
199672-07-6P 199672-08-7P 199672-10-1P
199672-11-2P 199672-13-4P 199672-15-6P
199672-20-3P 199672-21-4P 246177-94-6P
246177-95-7P 246177-96-8P
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

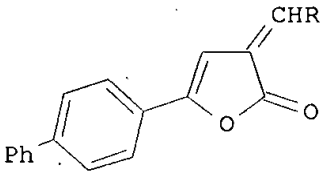
(Biological study); PREP (Preparation); USES (Uses)
(matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)

IT **179545-16-5P 179546-44-2P 199672-37-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(matrix metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)

IT **199672-24-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(metalloprotease-inhibiting biaryl acetylenes and their use as therapeutics)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:657381 HCAPLUS
DN 132:293296
TI Reactions of 3-(p-phenylbenzoyl)propionic acid with aromatic aldehydes and some nitrogen nucleophiles
AU Al-Haiza, M. A.; El-Assiery, S. A.; El-Kady, M.
CS Chemistry Department, College of Education, King Saud University, Abha, Saudi Arabia
SO Egypt. J. Chem. (1999), 42(1), 83-90
CODEN: EGJCA3; ISSN: 0449-2285
PB National Information and Documentation Centre
DT Journal
LA English
GI



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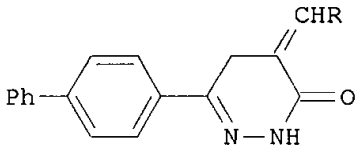
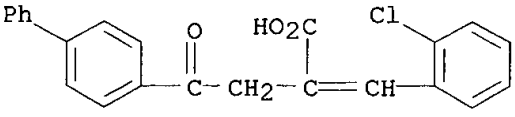


II

AB The title reactions were used to prep. heterocyclic compds. and other products. E.g., reaction of 3-(p-phenylbenzoyl)propionic acid with RCHO (R = 2-ClC6H4, 2-BrC6H4, 2-furyl) gave furanones I. Reaction of I with hydrazine hydrate gave pyridazinones II.

IT **264200-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(reactions of (phenylbenzoyl)propionic acid with arom. aldehydes and nitrogen nucleophiles)

RN 264200-01-3 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, .alpha.-[(2-chlorophenyl)methylene]-.gamma.-oxo- (9CI) (CA INDEX NAME)



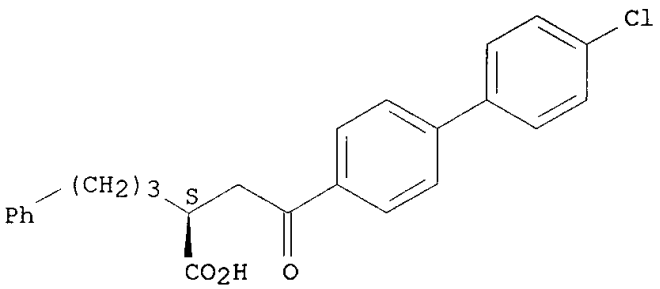
IT **264200-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(reactions of (phenylbenzoyl)propionic acid with arom. aldehydes and nitrogen nucleophiles)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:518319 HCAPLUS
DN 131:157647
TI Preparation of 4-biphenyl-4-hydroxybutyric acids as matrix metalloproteinase inhibitors
IN Kluender, Harold C. E.; Bjorge, Susan M.; Zadjura, Lisa Marie; Brubaker, William Frederick
PA Bayer Corporation, USA
SO U.S., 18 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5939583	A	19990817	US 1997-960921	19971030

OS MARPAT 131:157647
AB Title compds., e.g., (2S)-RZCH(OH)Z1CH(CO2H)(CH2)nZ2(CH2)mR1 [I; R = (un)substituted Ph; R1 = (hetero)aryl(alkenyl), phthalimido, Z3R8, etc.; R8 = (hetero)aryl(alkyl); Z = 1,4-phenylene; Z1,Z2 = CH2; Z1 = CH2 and Z2 = bond; Z3 = O or SO0-2; m = 0-4; n = 0 or 1] were prepd. Thus, (2S)-4-(4-ClC6H4)C6H4COCH2CH(CH2SPh)CO2H was reduced to give 2 diastereomers of (2S)-4-(4-ClC6H4)C6H4CH(OH)CH2CH(CH2SPh)CO2H. Data for biol. activity of I were given.
IT **179544-98-0**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); BIOL (Biological study)
(prepn. of 4-biphenyl-4-hydroxybutyric acids as matrix metalloproteinase inhibitors)
RN 179544-98-0 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



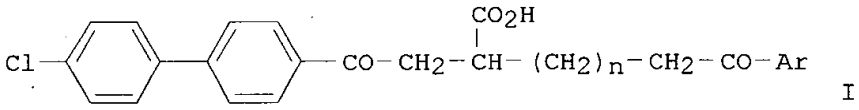
IT **179544-98-0**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); BIOL (Biological study)

(prepn. of 4-biphenyl-4-hydroxybutyric acids as matrix metalloproteinase inhibitors)
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:487140 HCAPLUS
DN 131:116074
TI Preparation of 2-(.omega.-aroylalkyl)-4-biaryl-4-oxobutyric acids as matrix metalloprotease inhibitors
IN Scott, William J.; Popp, Margaret A.; Hartsough, David S.
PA Bayer Corporation, USA
SO U.S., 20 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5932763	A	19990803	US 1997-856695	19970515

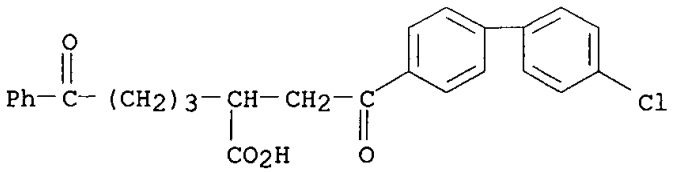
OS MARPAT 131:116074
GI



I

AB The present invention provides pharmaceutical compns. and methods for treating certain conditions comprising administering an amt. of a compd. or compn. of the invention which is effective to inhibit the activity of at least one matrix metalloprotease, resulting in achievement of the desired effect. The compds. of the present invention are of the generalized formula I [n is 1, 2, 3 or 4 and Ar represents a (substituted) arom. moiety]. These compds. are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempero mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plaque rupture. The present invention also provides pharmaceutical compns. and methods for treating such conditions. The title compd. I [n = 2; Ar = phenyl] in vitro showed IC50 of 65 nM against MMP-3.
IT **199329-29-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-(.omega.-aroylalkyl)-4-biaryl-4-oxobutyric acids as matrix metalloprotease inhibitors)
RN 199329-29-8 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-(4-oxo-4-

phenylbutyl)- (9CI) (CA INDEX NAME)



IT **199329-29-8P 199329-30-1P 199329-31-2P**
199329-32-3P 199329-33-4P 199329-34-5P
199329-35-6P 199329-36-7P 199329-37-8P
199329-38-9P 199329-39-0P 199329-40-3P
199329-43-6P 232940-97-5P 232940-98-6P
232940-99-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-(.omega.-aroylalkyl)-4-biaryl-4-oxobutyric acids as matrix metalloprotease inhibitors)

IT **199329-47-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 2-(.omega.-aroylalkyl)-4-biaryl-4-oxobutyric acids as matrix metalloprotease inhibitors)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:468334 HCAPLUS
DN 131:125454
TI Matrix metalloprotease (MMP)-13 selective inhibitors for treatment of arthritis deformans and other MMP-related diseases
IN McClure, Kim Francis; Lopresti-Morrow, Lori Lynn; Mitchell, Peter Geoffrey; Reeves, Lisa Marie; Reiter, Lawrence Alan; Robinson, Ralph Pelton; Yocum, Sue Ann
PA Pfizer Products Inc., USA
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11199512	A2	19990727	JP 1998-289540	19981012
	EP 935963	A2	19990818	EP 1998-308563	19981020
	EP 935963	A3	20001004		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2251197	AA	19990424	CA 1998-2251197	19981022
	AU 9889481	A1	19990520	AU 1998-89481	19981022
	ZA 9809667	A	20000425	ZA 1998-9667	19981023
PRAI	US 1997-62766	P	19971024		

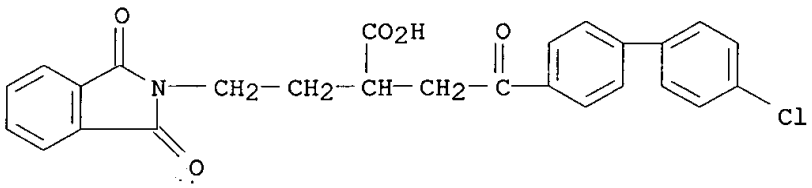
AB Matrix metalloprotease (MMP)-13 selective inhibitors including 1-{[4-(4-fluorophenoxy)benzenesulfonyl]-pyridin-3-ylmethylamino}-cyclopentanecarboxylic acid and other compds. and their pharmaceutically

acceptable salts are claimed for treatment of arthritis deformans and other MMP-related diseases. The inhibitory effects of these compds. on MMP 1 and MMP 13 were tested.

IT **179546-41-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix metalloprotease (MMP)-13 selective inhibitors for treatment of arthritis deformans and other MMP-related diseases)

RN 179546-41-9 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



IT **179546-41-9 179546-42-0**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix metalloprotease (MMP)-13 selective inhibitors for treatment of arthritis deformans and other MMP-related diseases)

L14 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:464012 HCAPLUS
DN 131:97624
TI MMP inhibitors for the treatment of ocular angiogenesis
IN Doherty, Niall Stephen
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 930067	A2	19990721	EP 1998-310351	19981216
	EP 930067	A3	19990915		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AU 9897224	A1	19990708	AU 1998-97224	19981218
	JP 11263735	A2	19990928	JP 1998-360567	19981218
	ZA 9811629	A	20000619	ZA 1998-11629	19981218
	JP 2001122775	A2	20010508	JP 2000-244194	19981218
PRAI	US 1997-68261	P	19971219		
	JP 1998-360567	A3	19981218		

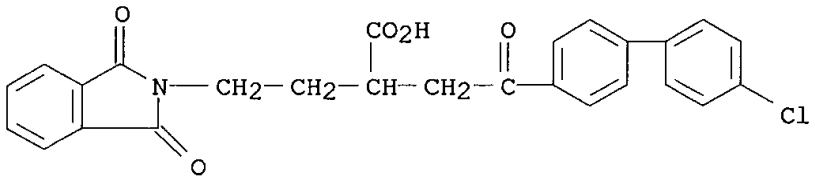
AB The present invention relates to the use of matrix metalloproteinase inhibitors, preferably those which display specificity for matrix metalloproteinases-2 or 9, in the treatment or prevention of ocular angiogenesis. Matrix metalloproteinase inhibitors are e.g. 3-[[4-[fluorophenoxy]benzenesulfonyl]-[1-hydroxycarbamoylcyclopentyl]amino]propionic acid and N-hydroxy-2-[4-phenylpiperidine-1-sulfonyl]acetamide.

IT **179546-41-9**

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MMP inhibitors for the treatment of ocular angiogenesis)

RN 179546-41-9 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



IT **179546-41-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MMP inhibitors for the treatment of ocular angiogenesis)

L14 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:450893 HCAPLUS

DN 131:101905

TI Inhibition of matrix metalloproteases by substituted biaryl oxobutyric acids

IN Vanzandt, Michael C.; Brittelli, David R.; Dixon, Brian R.

PA Bayer Corporation, USA

SO U.S., 27 pp.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5925637	A	19990720	US 1997-856693	19970515
	US 6225314	B1	20010501	US 1999-343142	19990629
PRAI	US 1997-856693	A3	19970515		

OS MARPAT 131:101905

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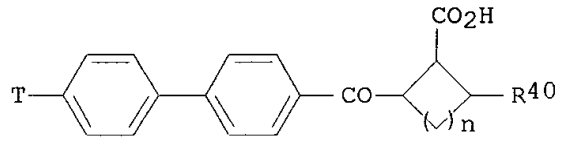

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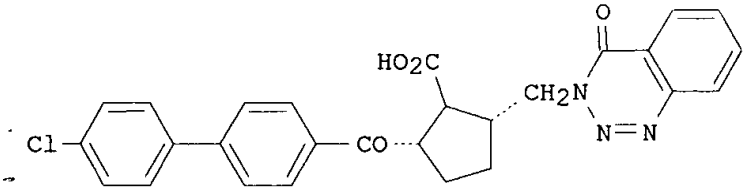

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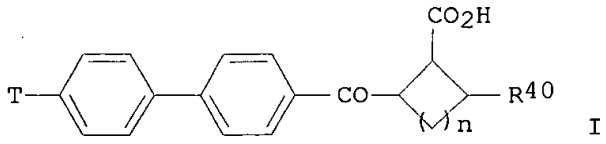

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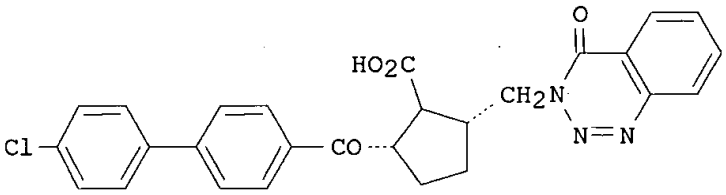


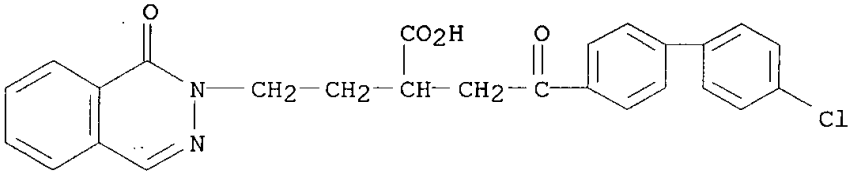
II

AB The title compds. I [n = 0-2; T = Cl, OBn, C.tplbond.CCH2OH, OCH2R (R = 4-pyridyl); R40 = mono- or biheterocyclic structure], matrix metalloprotease inhibitors, were prepd. Inhibition of MMP-2, MMP-3, and MMP-9 by I was detd. E.g., benzotriazinone deriv. II was prepd.

IT **199437-82-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of substituted biaryl oxobutyric acids and their inhibition of matrix metalloproteases)

RN 199437-82-6 HCAPLUS

CN 2(1H)-Phthalazinebutanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1-oxo- (9CI) (CA INDEX NAME)



IT **199437-82-6P 199437-84-8P 199437-86-0P 199437-88-2P 199437-90-6P 230959-73-6P 230959-76-9P 230959-77-0P 230959-78-1P 230959-79-2P 230959-80-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of substituted biaryl oxobutyric acids and their inhibition of matrix metalloproteases)

IT **199438-06-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of substituted biaryl oxobutyric acids and their inhibition of matrix metalloproteases)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

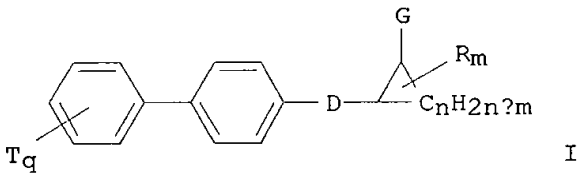
L14 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:205318 HCAPLUS

DN 130:267212
TI Biphenyl-derived substituted cycloalkanecarboxylic acid derivatives and analogs as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene; Bullock, William Harrison; Dixon, Brian Richard; Schneider, Stephan; Vanzandt, Michael Christopher; Wilhelm, Scott McClelland; Wolanin, Donald John
PA Bayer Corporation, USA
SO U.S., 102 pp., Cont. of U.S. Ser. No. 463,471, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5886022	A	19990323	US 1997-866568	19970530
PRAI	US 1995-463471		19950605		

OS MARPAT 130:267212
GI



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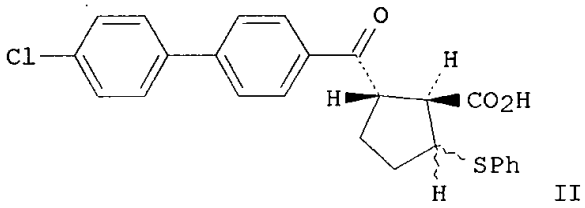


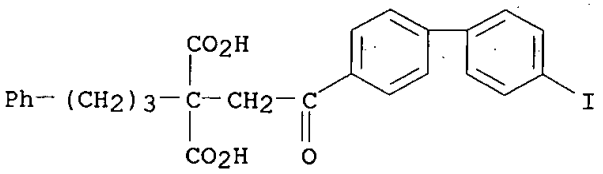
II

AB The invention discloses inhibitors for matrix metalloproteases (MMPs), pharmaceutical compns. contg. the inhibitors, and a process for using them to treat a variety of physiol. conditions. The claimed compds. have the generalized formula I [wherein each T = halo, alk(en/yn)yl, (CH2)pQ, etc.; Q = aryl, heteroaryl, cyano, CHO, NO2, etc.; p = 0-4; q = 0-2; D = CO, CH(OH), C:NOH, C:S; n = 2 or 3; R = alk(en/yn)yl, aralk(en/yn)yl; G = CO2H, alkoxycarbonyl, (di)(alkyl)carbamoyl, or amino acid residues bound at N via a CO linker; m = 0-2]. Approx. 250 compds. including both I and many acyclic carboxylic acid analogs were prepd. For instance, Friedel-Crafts acylation of 4-chlorobiphenyl by 1-cyclopentene-1,2-dicarboxylic anhydride, followed by lithiation/reprotonation to effect double-bond isomerization, and Michael addn. of thiophenol to the double bond, gave 2 diastereomers of title compd. II. The trans,trans isomer of II was the most active diastereomer, with IC50 values as follows: MMP-3 14-47 nM, MMP-9 56 nM, and MMP-2 4 nM.
IT **179547-85-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

RN 179547-85-4 HCAPLUS

CN Propanedioic acid, [2-(4'-iodo[1,1'-biphenyl]-4-yl)-2-oxoethyl](3-phenylpropyl)- (9CI) (CA INDEX NAME)



IT **179547-85-4P 179548-06-2P**, 2-Carboxy-5-phenyl-2-[2-oxo-2-(4'-chlorobiphenyl-4-yl)ethyl]pentanoic acid **179548-58-4P**, .alpha.-Carboxy-4'-chloro-.delta.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-pentanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

IT **179544-21-9P**, 4'-Iodo-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-23-1P 179544-28-6P 179544-30-0P 179544-39-9P**, 4'-Amino-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-55-9P**, 4'-Methoxy-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-65-1P**, 4'-Hydroxy-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179545-06-3P**, 4'-Nitro-.gamma.-oxo-.alpha.-(2-phenylethyl)[1,1'-biphenyl]-4-butanoic acid **179545-08-5P**, 4'-Chloro-.alpha.-[2-(2-iodophenyl)ethyl]-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

IT **179544-24-2P**, (E)-4'-(2-Carboxyethenyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-29-7P**, 4'-(1,1-Dimethylethyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-31-1P**, 4'-(Cyanomethyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-32-2P**, 4'-(Methylthio)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-33-3P**, 4'-(2-Chloroethoxy)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-34-4P**, 4'-(Hydroxymethyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-35-5P**, 4'-(2-Hydroxyethoxy)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-36-6P**, 4'-Ethenyl-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-37-7P**, 4'-Cyano-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-38-8P**, .gamma.-Oxo-.alpha.-(3-phenylpropyl)-4'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-butanoic acid **179544-41-3P**, 4'-(Aminomethyl)-.gamma.-oxo-

.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-42-4P 179544-44-6P**, .gamma.-Oxo-.alpha.-(3-phenylpropyl)-4'-(trifluoromethyl)[1,1'-biphenyl]-4-butanoic acid **179544-45-7P**, 4'-Nitro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-47-9P**, 3',4'-Dichloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-48-0P**, 3',5'-Dichloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-49-1P**, 4'-(Acetyloxy)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-56-0P**, 3'-Chloro-4'-fluoro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-57-1P**, 4'-Ethoxy-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-59-3P**, 2',4'-Dichloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-60-6P**, 4'-Formyl-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-61-7P**, .gamma.-Oxo-.alpha.-(3-phenylpropyl)-3',5'-bis(trifluoromethyl)[1,1'-biphenyl]-4-butanoic acid **179544-63-9P**, .gamma.-Oxo-.alpha.-(3-phenylpropyl)-3'-(trifluoromethyl)[1,1'-biphenyl]-4-butanoic acid **179544-64-0P**, 2'-Formyl-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-66-2P**, .gamma.-Oxo-.alpha.-(3-phenylpropyl)-4'-propoxy[1,1'-biphenyl]-4-butanoic acid **179544-67-3P**, .gamma.-Oxo-4'-(pentyloxy)-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-70-8P**, 4'-(Hexyloxy)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-71-9P**, 4'-Butoxy-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-72-0P**, .gamma.-Oxo-4'-(3-phenylpropoxy)-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-73-1P**, 4'-(1-Methylethoxy)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-74-2P**, 4'-(Heptyloxy)-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-97-9P**, (R)-4'-Chloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179544-98-0P**, (S)-4'-Chloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179545-07-4P**, 4'-Cyano-.gamma.-oxo-.alpha.-(2-phenylethyl)[1,1'-biphenyl]-4-butanoic acid **179545-13-2P**, 4'-Chloro-.gamma.-oxo-.alpha.-(phenylmethyl)[1,1'-biphenyl]-4-butanoic acid **179545-14-3P**, 4'-Chloro-.gamma.-oxo-.alpha.-(2-phenylethyl)[1,1'-biphenyl)-4-butanoic acid **179545-17-6P**, .gamma.-Oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179545-18-7P**, 4'-Amino-.gamma.-oxo-.alpha.-(2-phenylethyl)[1,1'-biphenyl]-4-butanoic acid hydrochloride **179545-24-5P**, 4'-Chloro-.alpha.-[2-[2-(methoxycarbonyl)phenyl]ethyl]-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid **179545-58-5P**, (S)-4'-Bromo-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid **179545-59-6P**, 4'-Chloro-.gamma.-oxo-.alpha.-(4-phenylbutyl)[1,1'-biphenyl]-4-butanoic acid **179545-60-9P**, 4'-Chloro-.gamma.-oxo-.alpha.-(5-phenylpentyl)[1,1'-biphenyl]-4-butanoic acid **179545-61-0P**, 4'-Chloro-.gamma.-oxo-.alpha.-(6-phenylhexyl)[1,1'-biphenyl]-4-butanoic acid **179545-62-1P**, .alpha.-([1,1'-Biphenyl]-4-ylmethyl)-4'-chloro-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid **179545-63-2P**, (E)-4'-Chloro-.gamma.-oxo-.alpha.-(3-phenyl-2-propenyl)[1,1'-biphenyl]-4-butanoic acid **179545-64-3P**, 4'-Chloro-.alpha.-[3-(4-methylphenyl)propyl]-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid **179545-65-4P**, 4'-Chloro-.alpha.-[3-(4-chlorophenyl)propyl]-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid **179545-66-5P**, 4'-Chloro-.alpha.-[3-(4-methoxyphenyl)propyl]-.gamma.-oxo[1,1'-biphenyl]-4-

butanoic acid **179545-67-6P**, 4'-Chloro-.alpha.-[2-(4-methoxyphenyl)ethyl]-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid **179545-68-7P**, 4'-Chloro-.alpha.-[2-(3-methoxyphenyl)ethyl]-.gamma.-oxo[1,1'-biphenyl]-4-butanoic acid **179545-69-8P**, 4'-Chloro-.gamma.-oxo-.alpha.-(3-phenyl-2-propynyl)[1,1'-biphenyl]-4-butanoic acid **179546-35-1P**, .alpha.-[2-(4'-Chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-pentanoic acid **179546-41-9P 179546-71-5P 179546-73-7P** **179546-88-4P**, 4'-Chloro-.delta.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-pentanoic acid
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

IT **179544-96-8P**, 4'-Chloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(resoln.; prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

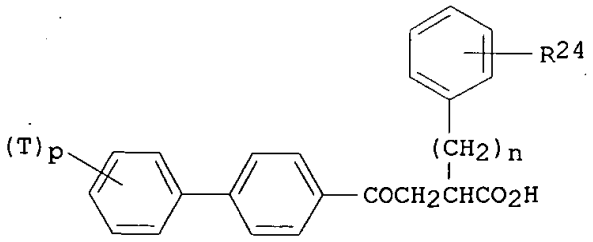
IT **179544-40-2P**, 4'-Amino-.gamma.-oxo-.alpha.-(3-phenylpropyl)[1,1'-biphenyl]-4-butanoic acid trifluoroacetate
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:590737 HCAPLUS
DN 129:230536
TI Inhibition of matrix metalloproteases by substituted phenalkyl compounds
IN Wolanin, Donald J.
PA Bayer Corp., USA
SO U.S., 22 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5804581	A	19980908	US 1997-856696	19970515

OS MARPAT 129:230536
GI



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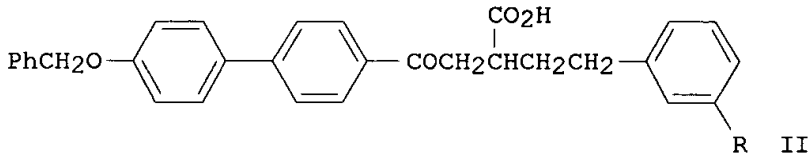


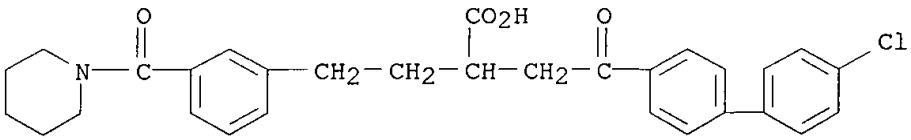
II

AB Matrix metalloprotease inhibiting compds., pharmaceutical compns. thereof and a method of disease treatment using such compds. are presented. The compds., i.e. 2-phenylalkyl-4-(1,1'-biphenyl-4-yl)-3-oxobutyric acid, of the invention have the generalized formula [I; T = halo, benzyloxy, C1-5 alkoxy; p = 1,2; n = an integer of 1-5; R24 = morpholinocarbonyl, N-(2-morpholinoethyl)carbamoyl, N-(3-phenylpropyl)carbamoyl, N-(2-phenylethyl)carbamoyl, N-(2-ethoxycarbonylethyl)carbamoyl, N-(ethoxycarbonylmethyl)carbamoyl, N-(2-carboxyethyl)carbamoyl, etc.]. These compds. are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis, bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempera mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plaque rupture. The present invention also provides pharmaceutical compns. and methods for treating such conditions. Palladium-mediated carbonylation of 4-(3-iodophenyl)butyric acid deriv. (II; R = iodo) by carbon monoxide and piperidine as the nucleophile in the presence of Pd(OAc)2 and 1,3-bis(diphenylphosphino)propane in DMSO gave the title compd. II (piperidine-1-carbonyl), which inhibited MMP-3, MMP-9, and MMP-2 with Ki of 12.5, 102, and 4.44 nM, resp.

IT **179547-77-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylalkyl(biphenylyl)oxobutyric acid derivs. as inhibitors of matrix metalloproteases for treating matrix metalloproteases-assocd. diseases)

RN 179547-77-4 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-[2-[3-(1-piperidinylcarbonyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



IT **179547-77-4P 199674-57-2P 199674-58-3P**
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199674-62-9P 199674-63-0P 199674-64-1P
199674-65-2P 199674-66-3P 199674-67-4P
199674-68-5P 199674-69-6P 199674-70-9P
199674-71-0P 199674-72-1P 199674-73-2P
199674-74-3P 199674-75-4P 199674-76-5P
199674-77-6P 199674-78-7P 199674-79-8P
199674-80-1P 199674-82-3P 199674-83-4P
199674-84-5P 199674-85-6P 199674-86-7P
199674-87-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylalkyl(biphenylyl)oxobutyric acid derivs. as inhibitors of matrix metalloproteases for treating matrix metalloproteases-assocd. diseases)

IT **179545-08-5P 199674-88-9P 212613-28-0P**
212613-29-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of phenylalkyl(biphenylyl)oxobutyric acid derivs. as inhibitors of matrix metalloproteases for treating matrix metalloproteases-assocd. diseases)

L14 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:534889 HCAPLUS
DN 129:161412
TI Derivatives of substituted 4-biarylbutyric acid as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; Wolanin, Donald John; Wilhelm, Scott M.
PA Bayer Corporation, USA
SO U.S., 109 pp. Cont.-in-part of U.S. Ser. No. 339,846.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5789434	A	19980804	US 1995-539409	19951106
	CA 2201863	AA	19960523	CA 1995-2201863	19951109
	CN 1163604	A	19971029	CN 1995-196209	19951109
	HU 78083	A2	19990830	HU 1998-233	19951109
	ZA 9509647	A	19970814	ZA 1995-9647	19951114
	TW 413675	B	20001201	TW 1995-84112045	19951114
	US 5874473	A	19990223	US 1997-864666	19970528
	US 5886024	A	19990323	US 1997-865325	19970528
	US 5854277	A	19981229	US 1997-865639	19970530

	US 5859047	A	19990112	US 1997-866798	19970530
	US 5861427	A	19990119	US 1997-866679	19970530
	US 5861428	A	19990119	US 1997-866680	19970530
	US 5886043	A	19990323	US 1997-866778	19970530
	US 6166082	A	20001226	US 1998-57679	19980409
PRAI	US 1994-339846	A2	19941115		
	US 1995-462729	B1	19950605		
	US 1995-463490	B1	19950605		
	US 1995-463580	B1	19950605		
	US 1995-463794	B1	19950605		
	US 1995-464253	B1	19950605		
	US 1995-465626	B1	19950605		
	US 1995-539409	A	19951106		

OS MARPAT 129:161412

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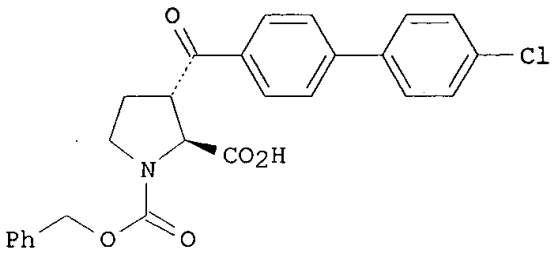


I

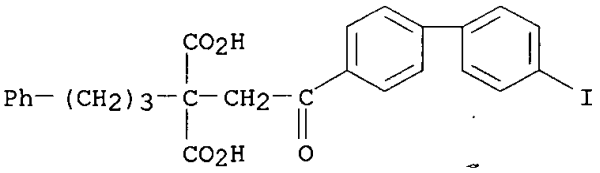
AB Matrix metalloprotease (MMP) inhibitors TxA-B-D-E-G [I; T = halo, haloalkyl, alkynyl, (un)substituted alkyl or alkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, 5-tetrazolyl, etc.] and their pharmaceutically acceptable salts were prepd. In particular, I [A = C6H4; B = 1,4-C6H4; E = certain substituted THF, tetrahydrothiophene, or pyrrolidine divalent radicals] with MMP inhibitory activity, and their pharmaceutically acceptable salts, are claimed. For instance, claimed title compd. II was prepd. from L-pyroglutaminol in 9 steps. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. For instance, II had corresponding IC50 values of 103, 381, and 35 nM. I inhibited tumor growth and metastasis in animal models, and inhibited cartilage lesions in a guinea pig model of osteoarthritis.

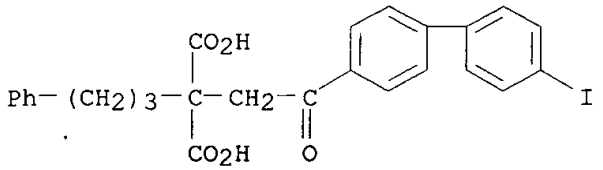
IT **179547-85-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179547-85-4 HCAPLUS

CN Propanedioic acid, [2-(4'-iodo[1,1'-biphenyl]-4-yl)-2-oxoethyl](3-phenylpropyl)- (9CI) (CA INDEX NAME)





IT **179547-85-4P 179548-06-2P 179548-14-2P**
179548-58-4P 179548-74-4P 179548-75-5P
179548-76-6P 179798-17-5P 188675-85-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179546-41-9P 179546-42-0P**
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179544-97-9P 179544-98-0P 179546-43-1P**
179546-72-6P 179798-05-1P 179798-06-2P
179798-07-3P
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179544-21-9P 179544-23-1P 179544-28-6P**
179544-30-0P 179544-37-7P 179544-40-2P
179544-55-9P 179544-65-1P 179545-06-3P
179545-08-5P 179545-18-7P 179545-24-5P
179545-36-9P 179545-37-0P 179545-44-9P
179545-45-0P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179544-24-2P 179544-29-7P 179544-31-1P**
179544-32-2P 179544-33-3P 179544-34-4P
179544-35-5P 179544-36-6P 179544-38-8P
179544-41-3P 179544-42-4P 179544-44-6P
179544-45-7P 179544-47-9P 179544-48-0P
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179547-42-3P 179547-44-5P 179547-45-6P
179547-46-7P 179547-47-8P 179547-48-9P
179547-49-0P 179547-50-3P 179547-51-4P
179547-52-5P 179547-53-6P 179547-54-7P
179547-55-8P 179547-56-9P 179547-57-0P
179547-58-1P 179547-59-2P 179547-60-5P
179547-61-6P 179547-62-7P 179547-63-8P
179547-64-9P 179547-68-3P 179547-70-7P
179547-77-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

L14 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:424117 HCAPLUS
DN 129:113523
TI Use of matrix metalloproteinase inhibitors for treating neurological disorders and promoting wound healing
IN Bocan, Thomas Michael Andrew; Boxer, Peter Alan; Peterson, Joseph Thomas, Jr.; Schrier, Denis; White, Andrew David
PA Warner-Lambert Co., USA; Bocan, Thomas Michael Andrew; Boxer, Peter Alan; Peterson, Joseph Thomas, Jr.; Schrier, Denis; White, Andrew David
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9826773	A1	19980625	WO 1997-US21532	19971121

W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9877353	A1	19980715	AU 1998-77353	19971121
	AU 737117	B2	20010809		
	EP 946166	A1	19991006	EP 1997-949584	19971121
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9714142	A	20000229	BR 1997-14142	19971121
	JP 2001507342	T2	20010605	JP 1998-527715	19971121
	ZA 9711279	A	19980623	ZA 1997-11279	19971215
	US 6340709	B1	20020122	US 1999-269123	19990319
PRAI	US 1996-32753	P	19961217		
	WO 1997-US21532	W	19971121		

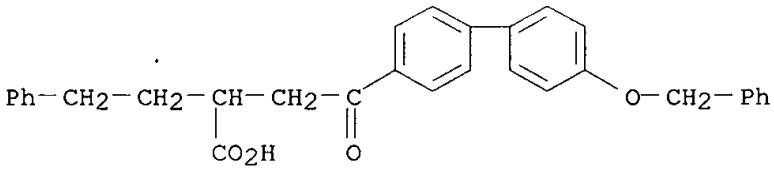
OS MARPAT 129:113523

AB Matrix metalloproteinase inhibitors 4-RC6H4SO2NHCHR1COR2 [R = (un)substituted Ph; R1 = alkyl, phenylalkyl, phenyl; R2 = OH, alkoxy, NHOH] and 4-RC6H4C(:NR3)CR4R5CR6R7COR8 [R3 = (un)substituted OH, NH2; R4-R7 = H, F, (un)substituted alkyl; R8 = OH, SH] are useful for preventing and treating neurol. disorders, esp. Alzheimer's, huntington's, and Parkinson's diease and amyotropic lateral sclerosis, and in promoting wound healing. IC50 for matrix metalloproteinase inhibition are reported for a no. of compds. Formulations contg. (R)-4-(4-NCC6H4)C6H4SO2NHCH(CO2H)CH2Ph, (S)-4-(4-H2NC6H4)C6H4SO2NHCH(CO2H)CH2C6H4OEt-3, and 4-(4-BrC6H4)C6H4SO2NHCH(CO2H)CHMe2 are reported.

IT **179545-43-8**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of matrix metalloproteinase inhibitors for treating neurol. disorders and promoting wound healing)

RN 179545-43-8 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, .gamma.-oxo-.alpha.-(2-phenylethyl)-4'-(phenylmethoxy)- (9CI) (CA INDEX NAME)



IT **179545-43-8 179546-45-3**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of matrix metalloproteinase inhibitors for treating neurol. disorders and promoting wound healing)

L14 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:379178 HCAPLUS
DN 129:40978
TI Racemization of substituted 4-ketocarboxylic acids.

IN Van Laak, Kai; Preiss, Michael
PA Bayer A.-G., Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19649827	A1	19980604	DE 1996-19649827	19961202
	WO 9824748	A1	19980611	WO 1997-EP6453	19971119
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9856540	A1	19980629	AU 1998-56540	19971119
	ZA 9710784	A	19980612	ZA 1997-10784	19971201
PRAI	DE 1996-19649827	A	19961202		
	WO 1997-EP6453	W	19971119		

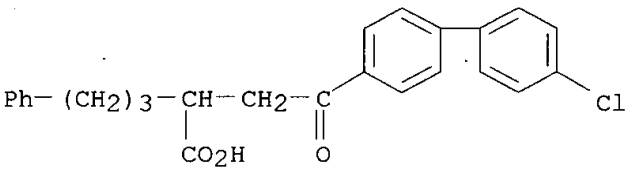
OS CASREACT 129:40978; MARPAT 129:40978

AB R1COCHR2CHR3CO2H [R1 = (substituted) aryl, diaryl; R2 = H, (substituted) alkyl, alkenyl; R3 = (substituted) alkyl, alkenyl], were racemized in an acid medium. Thus, (R)- or (S)-4-[4-(4-chlorophenyl)phenyl]-4-oxo-2-(3-phenylpropyl)butyric acid was refluxed in HCO2H; HBr was added and the mixt. was refluxed 5 h to give 98% 4-[4-(4-chlorophenyl)phenyl]-4-oxo-2-(3-phenylpropyl)butyric acid.

IT **179544-96-8P**, 4-[4-(4-Chlorophenyl)phenyl]-4-oxo-2-(3-phenylpropyl)butyric acid
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(racemization of substituted 4-ketocarboxylic acids)

RN 179544-96-8 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



IT **179544-96-8P**, 4-[4-(4-Chlorophenyl)phenyl]-4-oxo-2-(3-phenylpropyl)butyric acid **179546-41-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(racemization of substituted 4-ketocarboxylic acids)

IT **179544-97-9 179544-98-0 179546-42-0 179546-43-1**
RL: RCT (Reactant)
(racemization of substituted 4-ketocarboxylic acids)

L14 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:352815 HCAPLUS
DN 129:27819
TI Substituted 4-biphenyl-4-hydroxybutyric acid derivatives as matrix metalloprotease inhibitors
IN Kluender, Harold C. E.; Bjorge, Susan M.; Zadjura, Lisa Marie; Brubaker, William Frederick
PA Bayer Corp., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9822436	A1	19980528	WO 1997-US19960	19971030
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9851024	A1	19980610	AU 1998-51024	19971030
	AU 731830	B2	20010405		
	EP 937036	A1	19990825	EP 1997-945585	19971030
	EP 937036	B1	20011205		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9712707	A	19991026	BR 1997-12707	19971030
	ZA 9709756	A	19991101	ZA 1997-9756	19971030
	CN 1241177	A	20000112	CN 1997-180910	19971030
	JP 2001505877	T2	20010508	JP 1998-523677	19971030
	AT 210112	E	20011215	AT 1997-945585	19971030
	NO 9901994	A	19990615	NO 1999-1994	19990427
PRAI	US 1996-30264	P	19961031		
	WO 1997-US19960	W	19971030		

OS MARPAT 129:27819
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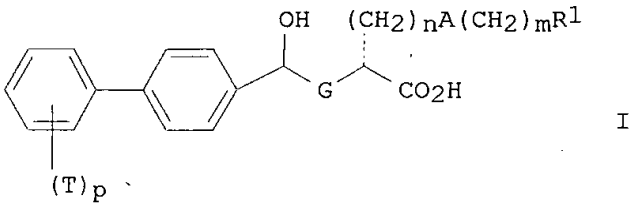


I

AB The title compds. I (T = pharmaceutically acceptable substituent group; p = 0-2; m = 0-4; n = 0, 1; A = CH2, CH, N; G = CH2, CH; R1 = substituent group; A and G may be joined), matrix metalloprotease inhibitors, were prepd. E.g., (S)-4-[4-(4-chlorophenyl)phenyl]-4-oxo-2-

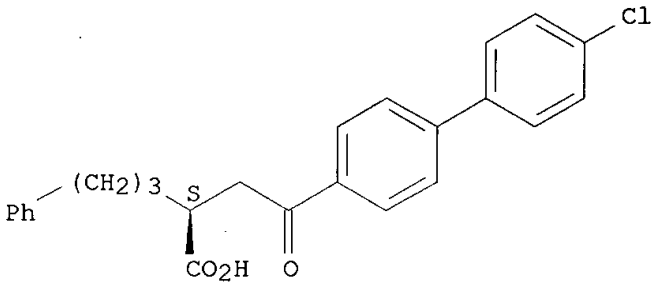
(phenylthiomethyl)butanoic acid was reduced with NaBH4 to give (2S,4R)- and (2S,4S)-4-[4-(4-chlorophenyl)phenyl]-4-hydroxy-2-(phenylthiomethyl)butanoic acids.

IT **179544-98-0P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylhydroxybutyric acid derivs. as matrix metalloprotease inhibitors)

RN 179544-98-0 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-(3-phenylpropyl)-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **179544-98-0P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylhydroxybutyric acid derivs. as matrix metalloprotease inhibitors)

L14 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:752921 HCAPLUS
DN 128:34585
TI Inhibition of matrix metalloproteases by substituted phenethyl compounds
IN Wolanin, Donald J.
PA Bayer Corporation, USA; Wolanin, Donald J.
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9743247	A1	19971120	WO 1997-US7919	19970512
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9704029	A	19980219	ZA 1997-4029	19970509

	AU 9729385	A1	19971205	AU 1997-29385	19970512
	AU 727899	B2	20010104		
	EP 907632	A1	19990414	EP 1997-923621	19970512
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9709084	A	19990803	BR 1997-9084	19970512
	CN 1225624	A	19990811	CN 1997-196457	19970512
	JP 11510517	T2	19990914	JP 1997-540979	19970512
PRAI	US 1996-645026	A2	19960515		
	WO 1997-US7919	W	19970512		

OS MARPAT 128:34585

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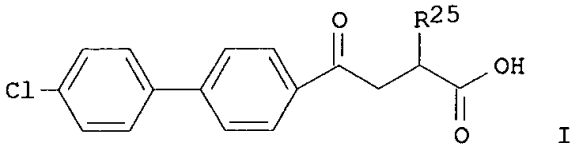

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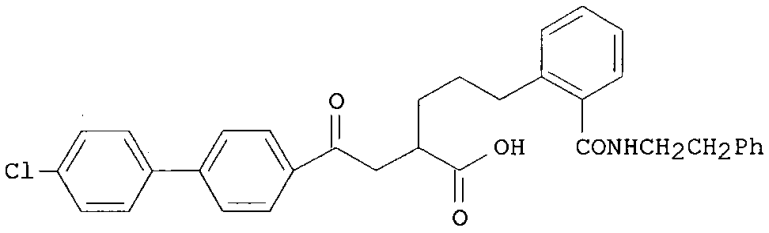


II

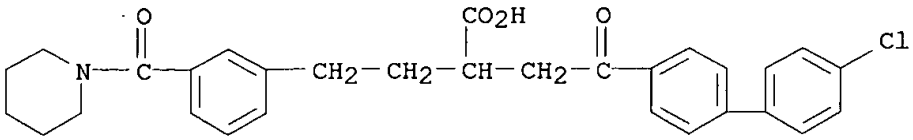
AB Matrix metalloprotease inhibiting compds., pharmaceutical compns. thereof and a method of disease treatment using such compds. are presented. The compds. of the invention have generalized formula I wherein R25 is a substituted phenylethyl moiety. These compds. are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempero mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plaque rupture. The present invention also provides pharmaceutical compns. and methods for treating such conditions. The title compd. II in vitro showed the Ki value of 127 nM against MMP-3.

IT **179547-77-4P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibition of matrix metalloproteases by substituted phenethyl compds.)

RN 179547-77-4 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-[2-[3-(1-piperidinylcarbonyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



IT **179547-77-4P 199674-57-2P 199674-58-3P**
199674-59-4P 199674-60-7P 199674-61-8P
199674-62-9P 199674-63-0P 199674-64-1P
199674-65-2P 199674-66-3P 199674-67-4P
199674-68-5P 199674-69-6P 199674-70-9P
199674-71-0P 199674-72-1P 199674-73-2P
199674-74-3P 199674-75-4P 199674-76-5P
199674-77-6P 199674-78-7P 199674-79-8P
199674-80-1P 199674-81-2P 199674-82-3P
199674-83-4P 199674-84-5P 199674-85-6P
199674-86-7P 199674-87-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibition of matrix metalloproteases by substituted phenethyl compds.)

IT **179545-08-5P 179545-45-0P 199674-88-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(inhibition of matrix metalloproteases by substituted phenethyl compds.)

L14 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:752919 HCAPLUS
DN 128:34581
TI Preparation of acetylene derivatives for inhibition of matrix metalloproteases
IN Dixon, Brian R.; Chen, Jinshan
PA Bayer Corporation, USA; Dixon, Brian R.; Chen, Jinshan
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9743245	A1	19971120	WO 1997-US7921	19970512
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9704031	A	19980219	ZA 1997-4031	19970509

	AU 9729386	A1	19971205	AU 1997-29386	19970512
	AU 710759	B2	19990930		
	EP 912496	A1	19990506	EP 1997-923622	19970512
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9709077	A	19990803	BR 1997-9077	19970512
	CN 1225623	A	19990811	CN 1997-196456	19970512
	JP 11511179	T2	19990928	JP 1997-540980	19970512
	JP 3090957	B2	20000925		
	TW 381079	B	20000201	TW 1997-86106283	19970512
PRAI	US 1996-645028	A2	19960515		
	WO 1997-US7921	W	19970512		

OS MARPAT 128:34581

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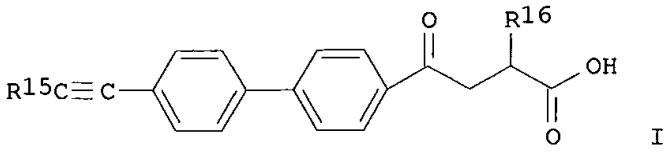

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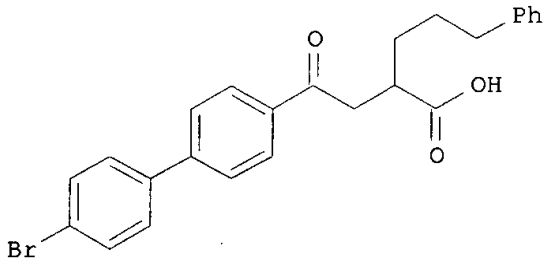


II

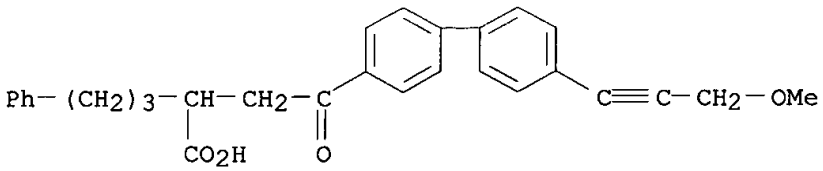
AB The title compds. [I; R15 = HOCH2, MeOCH2, CH3CO2CH2, EtOCO2CH2, HO(CH2)2, CH3CO2(CH2)2, HO2C(CH2)2, OHC(CH2)3, HO(CH2)4, Ph, etc.; R16 = Ph(CH2)3, phthalimidoethyl] are prepd. I are useful for inhibiting matrix metalloproteases and, therefore, combating conditions to which MMP's contribute, such as osteoarthritis, rheumatoid arthritis, septic arthritis, periodontal disease, corneal ulceration, proteinuria, aneurysmal aortic disease, dystrophobic epidermolysis, bullosa, conditions leading to inflammatory responses, osteopenias mediated by MMP activity, tempero mandibular joint disease, demyelating diseases of the nervous system, tumor metastasis or degenerative cartilage loss following traumatic joint injury, and coronary thrombosis from atherosclerotic plate rupture. Thus, compd. (II) was reacted with HOCH2C.tplbond.CH in the presence of Et2NH, CuI, and trans-dichlorobis(triphenylphosphine)palladate to give I [R15 = HOCH2, R16 = Ph(CH2)3], which showed IC50 of 21 .mu.M against MMP-3.

IT **179548-75-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acetylene derivs. for inhibition of matrix metalloproteases)

RN 179548-75-5 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, 4'-(3-methoxy-1-propynyl)-.gamma.-oxo-

.alpha.-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



IT **179548-75-5P 199671-99-3P 199672-01-0P**
199672-02-1P 199672-05-4P 199672-07-6P
199672-08-7P 199672-10-1P 199672-11-2P
199672-13-4P 199672-15-6P 199672-16-7P
199672-17-8P 199672-18-9P 199672-20-3P
199672-21-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acetylene derivs. for inhibition of matrix metalloproteases)

IT **179546-44-2P 199672-24-7P 199672-37-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of acetylene derivs. for inhibition of matrix metalloproteases)

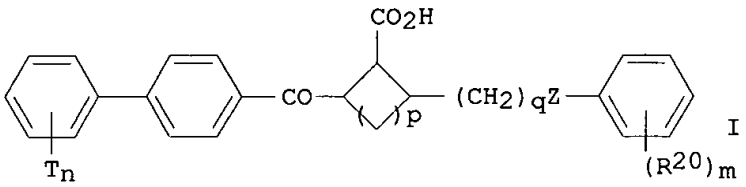
L14 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:752914 HCAPLUS
DN 128:22719
TI Inhibition of matrix metalloproteases by 2-(.omega.-aroylalkyl)-4-biaryloxobutyric acids
IN Scott, William J.; Popp, Margaret A.; Hartsough, David S.
PA Bayer Corporation, USA; Scott, William J.; Popp, Margaret A.; Hartsough, David S.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9743240	A1	19971120	WO 1997-US8608	19970512
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9704028	A	19980219	ZA 1997-4028	19970509
CA 2254750	AA	19971120	CA 1997-2254750	19970512
AU 9730104	A1	19971205	AU 1997-30104	19970512
AU 715877	B2	20000210		
EP 904260	A1	19990331	EP 1997-924788	19970512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9709078	A	19990803	BR 1997-9078	19970512

	CN 1234791	A	19991110	CN 1997-196453	19970512
	JP 2001509783	T2	20010724	JP 1997-541195	19970512
PRAI	US 1996-645029	A2	19960515		
	WO 1997-US8608	W	19970512		

OS MARPAT 128:22719

GI



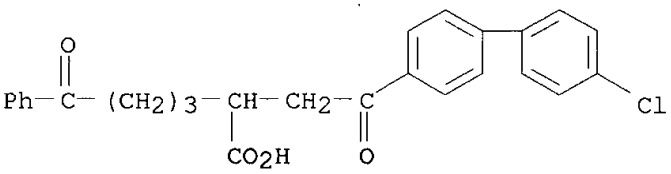
AB The title compds. I [q = 1-4; p = 0-2; n = 0-2; m = 0-3; Z = S, SO, SO2, CO, NR2CO, OC(O), O; T = F, Cl, Br, I, alkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, etc.; R20 = alkyl, alkoxy, aryloxy, halo, etc.; R2 = H, alkyl, aryl, etc.] were prepd. as matrix metalloprotease-inhibiting compds. E.g., 2-(2-(4-(4-chlorophenyl)phenyl)-2-oxoethyl)-6-phenyl-6-oxohexanoic acid was prepd. in several steps from malonic acid, 4-bromobutyrophenone, and 1-(4-(4-chlorophenyl)phenyl)-2-bromoethan-1-one.

IT **199329-29-8P**

RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (aroylalkyl)biaryloxobutyric acids as matrix metalloprotease-inhibiting compds.)

RN 199329-29-8 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-(4-oxo-4-phenylbutyl)- (9CI) (CA INDEX NAME)



IT **199329-29-8P 199329-30-1P 199329-31-2P**
199329-32-3P 199329-33-4P 199329-34-5P
199329-35-6P 199329-36-7P 199329-37-8P
199329-38-9P 199329-39-0P 199329-40-3P
199329-41-4P 199329-42-5P 199329-43-6P
199329-44-7P

RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (aroylalkyl)biaryloxobutyric acids as matrix metalloprotease-inhibiting compds.)

IT **199329-47-0P**

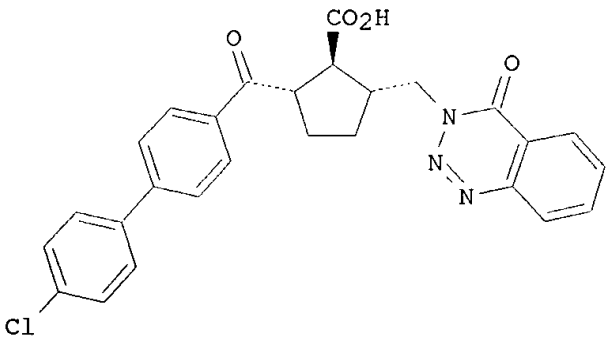
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of (aroylalkyl)biaryloxobutyric acids as matrix metalloprotease-inhibiting compds.)

L14 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:752913 HCAPLUS
DN 128:22927
TI Preparation of 1-azacycloalkylmethyl-5-(biphenylylcarbonyl)cyclopentanecarboxylates and analogs as matrix metalloprotease inhibitors
IN Van Zandt, Michael C.; Brittelli, David R.; Dixon, Brian R.
PA Bayer Corporation, USA; Van Zandt, Michael C.; Brittelli, David R.; Dixon, Brian R.
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743239	A1	19971120	WO 1997-US7976	19970512
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9704030	A	19980219	ZA 1997-4030	19970509
	CA 2254731	AA	19971120	CA 1997-2254731	19970512
	AU 9731220	A1	19971205	AU 1997-31220	19970512
	AU 714207	B2	19991223		
	EP 923530	A1	19990623	EP 1997-926455	19970512
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9709086	A	19990803	BR 1997-9086	19970512
	CN 1225621	A	19990811	CN 1997-196454	19970512
	JP 11510821	T2	19990921	JP 1997-541003	19970512
PRAI	US 1996-648493	A2	19960515		
	WO 1997-US7976	W	19970512		

OS MARPAT 128:22927
GI



II

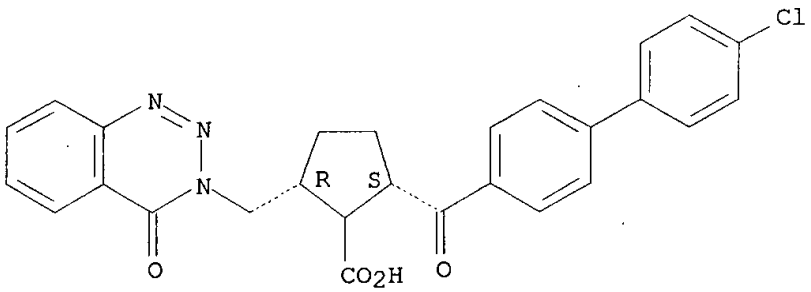
AB RZCOZ1R1 (Z = 4,4'-biphenyldiyl)[I; R = Cl, OCH2Ph, C.tplbond.CCH2OH, 4-pyridylmethoxy; R1 = e.g., oxodi- or -triazacycloalkylmethyl, etc.; Z1 = CH2CH(CO2H)CH2, 2-carboxy-1,3-cyclobut- or -pentanediyl] were prepd. Thus, the enol triflate of 2-trimethylsilylethyl oxobicyclo[2.2.1]heptane-7-carboxylate was arylated by 4'-chloro-4-trimethylstannylbiphenyl (prepn. each given) and the product ozonated to give, after redn., I [R = Cl, R1 = CH2OH, Z1 = 2-(2-trimethylsilylethoxycarbonyl)-1,3-cyclopentanediyl] which was aminated by 1,2,3-benzotriazin-4(3H)-one to give title compd. II. Data for biol. activity of I were given.

IT **199437-73-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-azacycloalkylmethyl-5-(biphenylylcarbonyl)cyclopentanecarboxylates and analogs as matrix metalloprotease inhibitors)

RN 199437-73-5 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl]-, (2R,5S)-rel-[partial]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **199437-73-5P 199437-76-8P 199437-77-9P**
199437-78-0P 199437-79-1P 199437-81-5P
199437-82-6P 199437-84-8P 199437-86-0P
199437-88-2P 199437-90-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-azacycloalkylmethyl-5-(biphenylylcarbonyl)cyclopentanecarboxylates and analogs as matrix metalloprotease inhibitors)

IT **199438-06-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 1-azacycloalkylmethyl-5-(biphenylylcarbonyl)cyclopentanecarboxylates and analogs as matrix metalloprotease inhibitors)

L14 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:24438 HCAPLUS
DN 126:157463
TI Heterocyclic compounds from 3-(4-phenylbenzoyl)propionic acid
AU Soliman, A.Y.; Bakeer, H.M.; Attia, I.A.
CS Science Department, Faculty of Teachers, Alhasa, 31982, Saudi Arabia
SO Chin. J. Chem. (1996), 14(6), 532-540
CODEN: CJOCEV; ISSN: 1001-604X

PB Science Press
DT Journal
LA English
GI

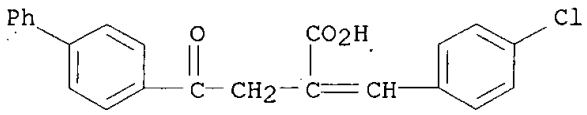
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 3-(4-Phenylbenzoyl)propionic acid was used as the starting material for the synthesis of furanones I (Ar = Ph, 4-ClC6H4, 4-MeOC6H4), pyrrolinones II (R = Cl, H, OMe, R' = Me, Et, 4-MeC6H4, Ph), pyridazinone III, benzoxazinone IV and quinazolinones, e.g., V. The behavior of the derivs. of furanones and benzoxazinones toward different nucleophiles is reported.

IT **186788-08-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of heterocyclic compds. from (phenylbenzoyl)propionic acid)

RN 186788-08-9 HCAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid, .alpha.-[(4-chlorophenyl)methylene]-.gamma.-oxo- (9CI) (CA INDEX NAME)



IT **186788-08-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of heterocyclic compds. from (phenylbenzoyl)propionic acid)

IT **186788-07-8P 186788-09-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of heterocyclic compds. from (phenylbenzoyl)propionic acid)

L14 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:476807 HCAPLUS
DN 125:142275
TI Substituted 4-biarylbutyric or 5-biarylpentanoic acids and derivatives as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; et al.
PA Bayer A.-G., USA
SO PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9615096	A1	19960523	WO 1995-US14002	19951109

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,

TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	CA 2201863	AA	19960523	CA 1995-2201863	19951109
	AU 9641975	A1	19960606	AU 1996-41975	19951109
	AU 702317	B2	19990218		
	EP 790974	A1	19970827	EP 1995-940572	19951109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	BR 9509686	A	19970930	BR 1995-9686	19951109
	CN 1163604	A	19971029	CN 1995-196209	19951109
	JP 10509146	T2	19980908	JP 1995-516097	19951109
	HU 78083	A2	19990830	HU 1998-233	19951109
	RU 2159761	C2	20001127	RU 1997-110108	19951109
	ZA 9509647	A	19970814	ZA 1995-9647	19951114
	FI 9702062	A	19970714	FI 1997-2062	19970514
	NO 9702220	A	19970714	NO 1997-2220	19970514
	US 5874473	A	19990223	US 1997-864666	19970528
	US 5886024	A	19990323	US 1997-865325	19970528
	US 5854277	A	19981229	US 1997-865639	19970530
	US 5859047	A	19990112	US 1997-866798	19970530
	US 5861427	A	19990119	US 1997-866679	19970530
	US 5861428	A	19990119	US 1997-866680	19970530
	US 5886043	A	19990323	US 1997-866778	19970530
PRAI	US 1994-339846	A	19941115		
	US 1995-462729	B1	19950605		
	US 1995-463490	B1	19950605		
	US 1995-463580	B1	19950605		
	US 1995-463794	B1	19950605		
	US 1995-464253	B1	19950605		
	US 1995-465626	B1	19950605		
	WO 1995-US14002	W	19951109		

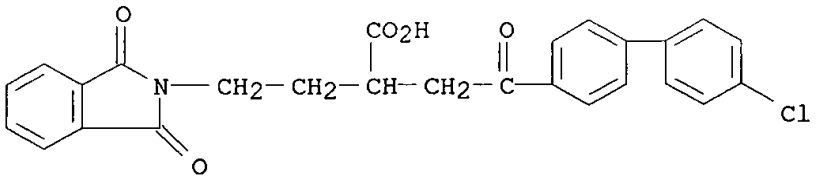
OS MARPAT 125:142275

AB Matrix metalloprotease inhibitors TxA-B-D-E-G [Tx = substituent such as halo, C1-C10 alkyl, or cyanoalkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, etc.] and their pharmaceutically acceptable salts were prepd. Thus, (S)-.gamma.-oxo-4'-(pentyloxy)-.alpha.-(3-phenylpropyl)-[1,1'-biphenyl]-4-butanoic acid (86) was prepd. via alkylation of di-Et (3-phenylpropyl)malonate with 2,4'-dibromoacetophenone, followed by sapon.-monodecarboxylation, reaction with 4-methoxybenzeneboronic acid, Me ether cleavage, and O-pentylation. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. Using compds. such as 86, the no. of tumor metastases was decreased between 38 and 49% as compared to the control. The title compds. were also assayed for inhibition of cartilage lesions in a guinea pig model of osteoarthritis.

IT **179546-41-9P**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179546-41-9 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



IT **179546-41-9P**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179544-21-9P 179544-23-1P 179544-28-6P**
179544-30-0P 179544-37-7P 179544-40-2P
179544-55-9P 179544-65-1P 179545-06-3P
179545-08-5P 179545-18-7P 179545-24-5P
179545-36-9P 179545-37-0P 179545-44-9P
179545-45-0P
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179546-42-0P**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); RCT (Reactant); SPN (Synthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179544-24-2P 179544-29-7P 179544-31-1P**
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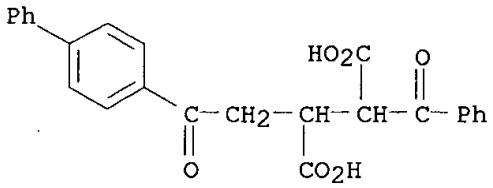
179547-31-0P 179547-32-1P 179547-35-4P
179547-36-5P 179547-37-6P 179547-41-2P
179547-42-3P 179547-44-5P 179547-45-6P
179547-46-7P 179547-47-8P 179547-48-9P
179547-49-0P 179547-50-3P 179547-51-4P
179547-52-5P 179547-53-6P 179547-54-7P
179547-55-8P 179547-56-9P 179547-57-0P
179547-58-1P 179547-59-2P 179547-60-5P
179547-61-6P 179547-62-7P 179547-63-8P
179547-64-9P 179547-68-3P 179547-70-7P
179547-77-4P
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179544-97-9P 179544-98-0P 179546-43-1P**
179546-72-6P 179798-05-1P 179798-06-2P
179798-07-3P
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); SPN (Synthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

IT **179547-85-4P 179548-06-2P 179548-14-2P**
179548-58-4P 179548-74-4P 179548-75-5P
179548-76-6P 179798-17-5P 188675-85-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

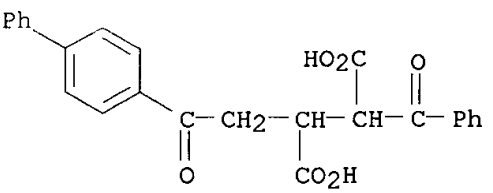
L14 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:116255 HCAPLUS
DN 124:260920
TI Heterocyclic compounds from alkylated 3-(4-phenylbenzoyl)acrylic acid
AU Soliman, A. Y.; Mohamed, F. K.; Mahamoud, M. R.
CS Faculty Education, Cairo University, Fayoum, Egypt
SO Bull. Fac. Sci., Assiut Univ., B (1995), 24(1), 299-309
CODEN: BFSAE6; ISSN: 1010-2671

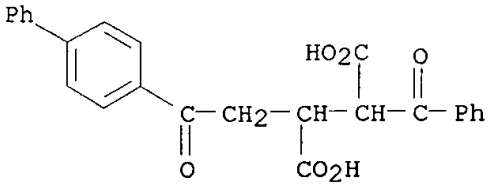
DT Journal
LA English
AB Pyrazole, pyridazine, pyrazolylpyridazine and pyrazolylthiopyridazine derivs. were synthesized utilizing 3-(4-phenylbenzoyl)acrylic acid as starting material.
IT **161037-93-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 161037-93-0 HCAPLUS
CN Butanedioic acid, 2-benzoyl-3-(2-[1,1'-biphenyl]-4-yl-2-oxoethyl)- (9CI) (CA INDEX NAME)



IT **161037-93-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

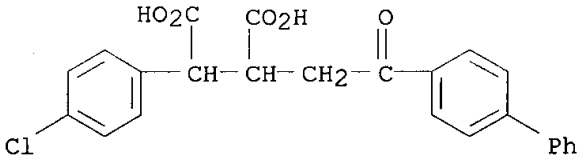
L14 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:297158 HCAPLUS
DN 122:133056
TI Heterocyclic compounds from alkylated products of 3-(4-phenylbenzoyl)acrylic acid
AU Soliman, A. Y.; Mahmoud, M. R.; Mohamed, F. K.
CS Faculty Sci., Ain Shams Univ., Cario, Egypt
SO Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem. (1995), 34B(1), 57-60
CODEN: IJSBDB; ISSN: 0376-4699
DT Journal
LA English
OS CASREACT 122:133056
AB Pyrazole, pyridazine, pyrazolylpyridazine and pyrzolylthiopyridazine derivs. have been synthesized utilizing 3-(4-phenylbenzoyl)acrylic acid as starting material.
IT **161037-93-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 161037-93-0 HCAPLUS
CN Butanedioic acid, 2-benzoyl-3-(2-[1,1'-biphenyl]-4-yl-2-oxoethyl)- (9CI) (CA INDEX NAME)





IT **161037-93-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

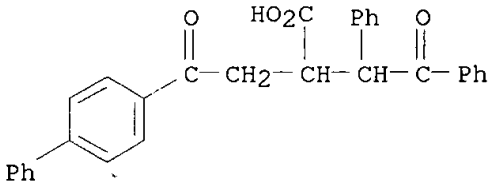
L14 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:94047 HCAPLUS
DN 108:94047
TI Alkylation reaction and Michael condensation of 3-aroylacrylic acids
AU Tamam, G. H.; Hamed, A. A.; El-Mobyed, M.; Mohamed, A. Y.
CS Fac. Sci., Ain Shams Univ., Cairo, Egypt
SO Egypt. J. Chem. (1986), Volume Date 1985, 28(4), 331-9
CODEN: EGJCA3; ISSN: 0367-0422
DT Journal
LA English
OS CASREACT 108:94047
AB p-Xylene and MeCOEt were alkylated by 4-PhC6H4COCH:CHCO2H to give 4-PhC6H4COCH2CHR1CO2H (R1 = 2,5-Me2C6H3, CHMeCOMe). Similarly, R2COCH:CHCO2H (R2 = PhC6H4, MeBrC6H3) and R3CH2CN (R3 = halophenyl, naphthyl, tolyl) gave succinic acids R2COCH2CH(CO2H)CHR3CO2H. A pyridazinone deriv. was prepd. from BrMeC6H3COCH:CHCO2H and N2H4.
IT **54469-86-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 54469-86-2 HCAPLUS
CN Butanedioic acid, 2-(2-[1,1'-biphenyl]-4-yl-2-oxoethyl)-3-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



IT **54469-86-2P 112982-64-6P 112982-65-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L14 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1975:31084 HCAPLUS
DN 82:31084
TI Michael reaction with .beta.-aroylacrylic acids
AU Sammour, A.; El-Hashash, M.
CS Fac. Sci., Ain Shams Univ., Cairo, Egypt
SO Egypt. J. Chem. (1973), 16(5), 381-93
CODEN: EGJCA3

DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB Michael adducts RCOCH2CHR1CO2H [I, R = Ph, p-MeC6H4, p-Ph-C6H4, tetrahydro-2-naphthyl; R1 = 1-oxo-2-cyclohexyl, 1-oxo-2-methyl-2-cyclohexyl, 1-oxo-2-cyclopentyl, 3-camphoryl, 1,3-diphenyl-5-oxo-2-pyrazolin-4-yl, CHPhCOPh, CHPhCO2H, CH-(C6H4Cl-p)CO2H, CHBz2] were prepd. in 62-79% yield by Michael condensation of RCOCH:CHCO2H with the appropriate ketone or nitrile. The butenolides II (R1 = 1-oxo-2-cyclohexyl, 1-oxo-2-methyl-2-cyclohexyl, 3-camphoryl, CHPhCOPh; R2 = H, Ph Me) were formed on acid cyclization of I. Reaction of I with hydrazines led either to the hydrazones of the oxo group of R1 or to dihydro-1,2-diazepines.
IT **54469-84-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 54469-84-0 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, .gamma.-oxo-.alpha.-(2-oxo-1,2-diphenylethyl)- (9CI) (CA INDEX NAME)



IT **54469-84-0P 54469-86-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

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L3        139029 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND NR>2 AND NRS>2
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L5               STR
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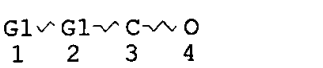


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GGCAT   IS MCY  UNS  AT   5
GGCAT   IS MCY  AT   6
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E6 C  AT   5
ECOUNT  IS E4 C  E1 S  AT   6

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   6

STEREO ATTRIBUTES: NONE
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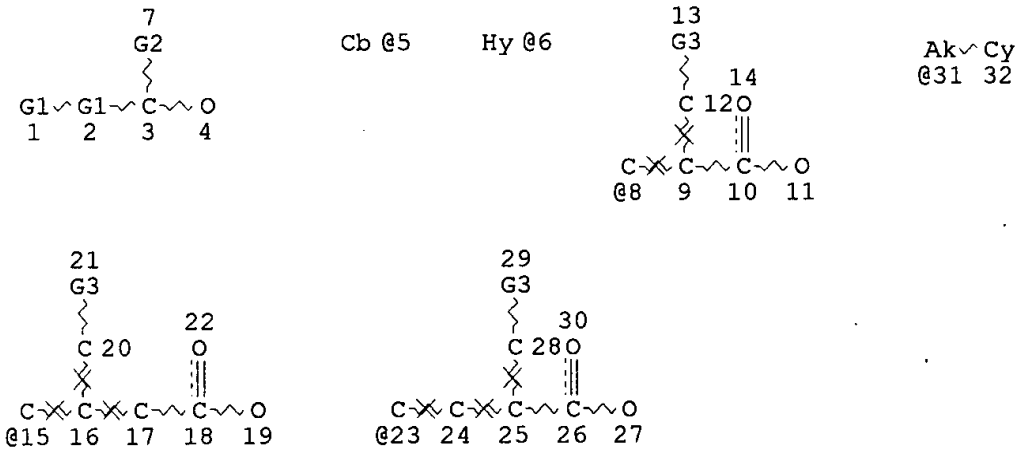


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VAR G2=8/15/23
VAR G3=CY/31
NODE ATTRIBUTES:
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CONNECT IS E1  RC AT  11
CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  27
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY  UNS  AT   5
GGCAT   IS MCY  AT   6
DEFAULT ECLEVEL IS LIMITED
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ECOUNT IS E6 C AT 5
ECOUNT IS E4 C E1 S AT 6

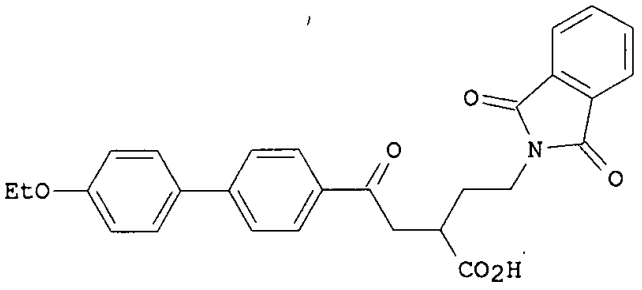
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L12 6 SEA FILE=REGISTRY SUB=L7 SSS FUL L10
L13 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L12

L13 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:475626 HCAPLUS
DN 133:89429
TI Preparation of 4-aryl-4-oxo-2-(2-phthalimidoethyl)butanoates and analogs as matrix metalloprotease inhibitors
IN Fitzgerald, Mary F.; Gardiner, Philip J.; Nash, Kevin; Sturton, Graham; Benz, Gunter; Henning, Rolf; Schlemmer, Karl-Heinz; Riedl, Bernd; Haning, Helmut
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000040539	A1	20000713	WO 1999-EP10110	19991220
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1140768	A1	20011010	EP 1999-963582	19991220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9916669	A	20011016	BR 1999-16669	19991220
PRAI	GB 1998-28845	A	19981230		
	GB 1999-22709	A	19990924		
	WO 1999-EP10110	W	19991220		

OS MARPAT 133:89429
GI



II

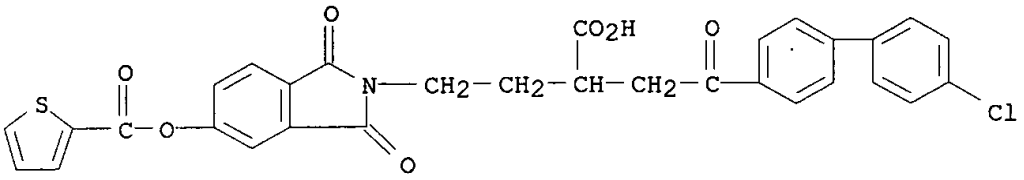
AB RZZ1Z2CO2H [I; R = (un)substituted Ph or -heteroaryl; Z = bond, (un)substituted 1,4-phenylene, -heteroarylene; Z1 = CO, CH(OH), C(:NOH), etc.; Z2 = substituted (CH2)2-3] were prepd. Thus, di-tert-Bu 2-(2-phthalimidoethyl)malonate was condensed with 4-(EtO)C6H4C6H4(COCH2Br)-

4 (prepn. each given) and the sapond. product mono-decarboxylated to give title compd. II. Data for biol. activity of I were given.

IT **179547-63-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-aryl-4-oxo-2-(2-phthalimidoethyl)butanoates and analogs as matrix metalloprotease inhibitors)

RN 179547-63-8 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-5-[(2-thienylcarbonyl)oxy]- (9CI) (CA INDEX NAME)

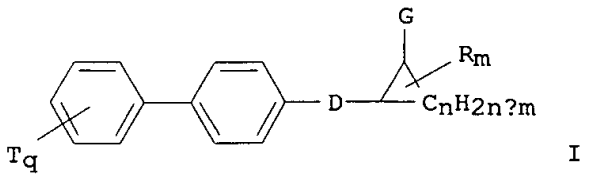


RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

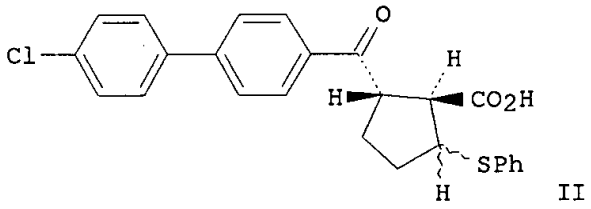
L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:205318 HCAPLUS
DN 130:267212
TI Biphenyl-derived substituted cycloalkanecarboxylic acid derivatives and analogs as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene; Bullock, William Harrison; Dixon, Brian Richard; Schneider, Stephan; Vanzandt, Michael Christopher; Wilhelm, Scott McClelland; Wolanin, Donald John
PA Bayer Corporation, USA
SO U.S., 102 pp., Cont. of U.S. Ser. No. 463,471, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5886022	A	19990323	US 1997-866568	19970530
PRAI	US 1995-463471		19950605		

OS MARPAT 130:267212
GI



I



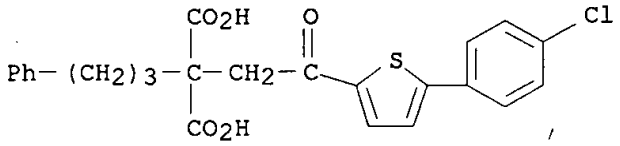
II

AB The invention discloses inhibitors for matrix metalloproteases (MMPs), pharmaceutical compns. contg. the inhibitors, and a process for using them to treat a variety of physiol. conditions. The claimed compds. have the generalized formula I [wherein each T = halo, alk(en/yn)yl, (CH2)pQ, etc.; Q = aryl, heteroaryl, cyano, CHO, NO2, etc.; p = 0-4; q = 0-2; D = CO, CH(OH), C:NOH, C:S; n = 2 or 3; R = alk(en/yn)yl, aralk(en/yn)yl; G = CO2H, alkoxycarbonyl, (di)(alkyl)carbamoyl, or amino acid residues bound at N via a CO linker; m = 0-2]. Approx. 250 compds. including both I and many acyclic carboxylic acid analogs were prepd. For instance, Friedel-Crafts acylation of 4-chlorobiphenyl by 1-cyclopentene-1,2-dicarboxylic anhydride, followed by lithiation/reprotonation to effect double-bond isomerization, and Michael addn. of thiophenol to the double bond, gave 2 diastereomers of title compd. II. The trans,trans isomer of II was the most active diastereomer, with IC50 values as follows: MMP-3 14-47 nM, MMP-9 56 nM, and MMP-2 4 nM.

IT **179548-72-2P**, .alpha.-Carboxy-5-(4-chlorophenyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)-2-thiophenebutanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

RN 179548-72-2 HCAPLUS

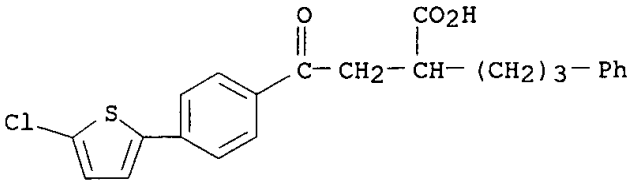
CN Propanedioic acid, [2-[5-(4-chlorophenyl)-2-thienyl]-2-oxoethyl](3-phenylpropyl)- (9CI) (CA INDEX NAME)



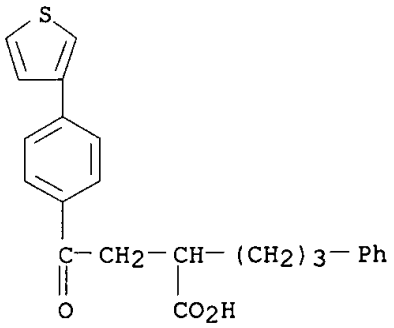
IT **179544-50-4P**, .alpha.-[2-[4-(5-Chloro-2-thienyl)phenyl]-2-oxoethyl]benzenepentanoic acid **179544-58-2P**, .alpha.-[2-Oxo-2-[4-(3-thienyl)phenyl]ethyl]benzenepentanoic acid **179544-62-8P**, .alpha.-[2-Oxo-2-[4-(2-thienyl)phenyl]ethyl]benzenepentanoic acid **179546-96-4P**, 5-(4-Chlorophenyl)-.gamma.-oxo-

.alpha.-(3-phenylpropyl)-2-thiophenebutanoic acid
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenyl-contg. substituted cycloalkanecarboxylic acid derivs. and acyclic analogs as matrix metalloprotease inhibitors)

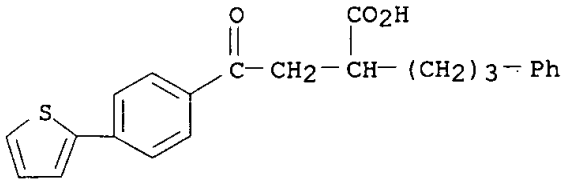
RN 179544-50-4 HCAPLUS
CN Benzenepentanoic acid, .alpha.-[2-[4-(5-chloro-2-thienyl)phenyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)



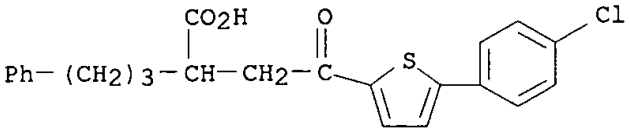
RN 179544-58-2 HCAPLUS
CN Benzenepentanoic acid, .alpha.-[2-oxo-2-[4-(3-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 179544-62-8 HCAPLUS
CN Benzenepentanoic acid, .alpha.-[2-oxo-2-[4-(2-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 179546-96-4 HCAPLUS
CN 2-Thiophenebutanoic acid, 5-(4-chlorophenyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)- (9CI) (CA INDEX NAME)

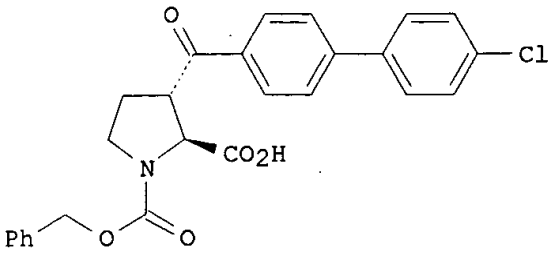


RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:534889 HCAPLUS
DN 129:161412
TI Derivatives of substituted 4-biarylbutyric acid as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; Wolanin, Donald John; Wilhelm, Scott M.
PA Bayer Corporation, USA
SO U.S., 109 pp. Cont.-in-part of U.S. Ser. No. 339,846.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5789434	A	19980804	US 1995-539409	19951106
	CA 2201863	AA	19960523	CA 1995-2201863	19951109
	CN 1163604	A	19971029	CN 1995-196209	19951109
	HU 78083	A2	19990830	HU 1998-233	19951109
	ZA 9509647	A	19970814	ZA 1995-9647	19951114
	TW 413675	B	20001201	TW 1995-84112045	19951114
	US 5874473	A	19990223	US 1997-864666	19970528
	US 5886024	A	19990323	US 1997-865325	19970528
	US 5854277	A	19981229	US 1997-865639	19970530
	US 5859047	A	19990112	US 1997-866798	19970530
	US 5861427	A	19990119	US 1997-866679	19970530
	US 5861428	A	19990119	US 1997-866680	19970530
	US 5886043	A	19990323	US 1997-866778	19970530
	US 6166082	A	20001226	US 1998-57679	19980409
PRAI	US 1994-339846	A2	19941115		
	US 1995-462729	B1	19950605		
	US 1995-463490	B1	19950605		
	US 1995-463580	B1	19950605		
	US 1995-463794	B1	19950605		
	US 1995-464253	B1	19950605		
	US 1995-465626	B1	19950605		
	US 1995-539409	A	19951106		

OS MARPAT 129:161412
GI



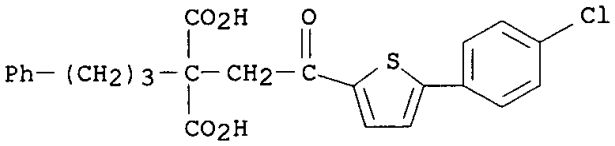
I

AB Matrix metalloprotease (MMP) inhibitors TxA-B-D-E-G [I; T = halo, haloalkyl, alkynyl, (un)substituted alkyl or alkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, 5-tetrazolyl, etc.] and their pharmaceutically acceptable salts were prepd. In particular, I [A = C6H4; B = 1,4-C6H4; E = certain substituted THF, tetrahydrothiophene, or pyrrolidine divalent radicals] with MMP inhibitory activity, and their pharmaceutically acceptable salts, are claimed. For instance, claimed title compd. II was prepd. from L-pyroglutaminol in 9 steps. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. For instance, II had corresponding IC50 values of 103, 381, and 35 nM. I inhibited tumor growth and metastasis in animal models, and inhibited cartilage lesions in a guinea pig model of osteoarthritis.

IT **179548-72-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179548-72-2 HCAPLUS

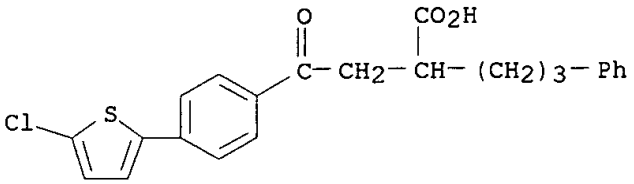
CN Propanedioic acid, [2-[5-(4-chlorophenyl)-2-thienyl]-2-oxoethyl](3-phenylpropyl)- (9CI) (CA INDEX NAME)



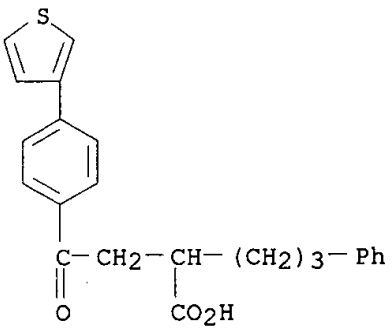
IT **179544-50-4P 179544-58-2P 179544-62-8P**
179546-96-4P 179547-63-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179544-50-4 HCAPLUS

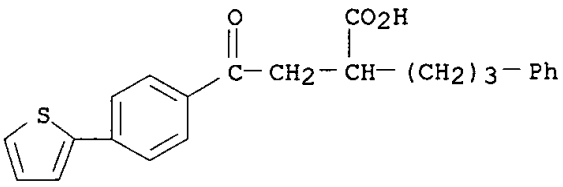
CN Benzenepentanoic acid, .alpha.-[2-[4-(5-chloro-2-thienyl)phenyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)



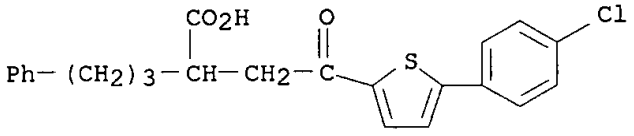
RN 179544-58-2 HCAPLUS
CN Benzenepentanoic acid, .alpha.-[2-oxo-2-[4-(3-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



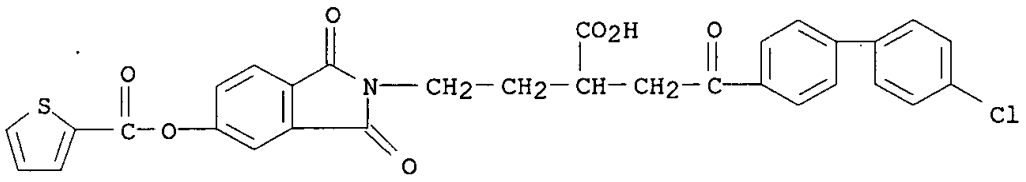
RN 179544-62-8 HCAPLUS
CN Benzenepentanoic acid, .alpha.-[2-oxo-2-[4-(2-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 179546-96-4 HCAPLUS
CN 2-Thiophenebutanoic acid, 5-(4-chlorophenyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



RN 179547-63-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-5-[(2-thienylcarbonyl)oxy]- (9CI) (CA INDEX NAME)



L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:476807 HCAPLUS
DN 125:142275
TI Substituted 4-biarylbutyric or 5-biarylpentanoic acids and derivatives as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt, Michael Christopher; et al.
PA Bayer A.-G., USA
SO PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9615096	A1	19960523	WO 1995-US14002	19951109
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	AU 9641975	A1	19960606	AU 1996-41975	19951109
	AU 702317	B2	19990218		
	EP 790974	A1	19970827	EP 1995-940572	19951109
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	BR 9509686	A	19970930	BR 1995-9686	19951109
	CN 1163604	A	19971029	CN 1995-196209	19951109
	JP 10509146	T2	19980908	JP 1995-516097	19951109
	HU 78083	A2	19990830	HU 1998-233	19951109
	RU 2159761	C2	20001127	RU 1997-110108	19951109
	ZA 9509647	A	19970814	ZA 1995-9647	19951114
	FI 9702062	A	19970714	FI 1997-2062	19970514
	NO 9702220	A	19970714	NO 1997-2220	19970514
	US 5874473	A	19990223	US 1997-864666	19970528
	US 5886024	A	19990323	US 1997-865325	19970528
	US 5854277	A	19981229	US 1997-865639	19970530
	US 5859047	A	19990112	US 1997-866798	19970530
	US 5861427	A	19990119	US 1997-866679	19970530
	US 5861428	A	19990119	US 1997-866680	19970530
	US 5886043	A	19990323	US 1997-866778	19970530
PRAI	US 1994-339846	A	19941115		
	US 1995-462729	B1	19950605		

	US 1995-463490	B1	19950605
	US 1995-463580	B1	19950605
	US 1995-463794	B1	19950605
	US 1995-464253	B1	19950605
	US 1995-465626	B1	19950605
	WO 1995-US14002	W	19951109

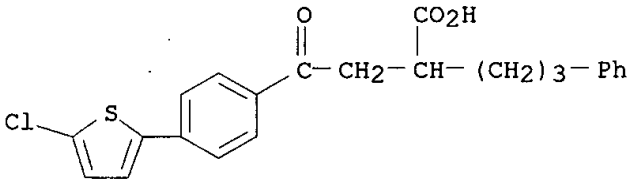
OS MARPAT 125:142275

AB Matrix metalloprotease inhibitors TxA-B-D-E-G [Tx = substituent such as halo, C1-C10 alkyl, or cyanoalkenyl; x = 0, 1, 2; A, B = arom. or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, etc.] and their pharmaceutically acceptable salts were prepd. Thus, (S)-.gamma.-oxo-4'-(pentyloxy)-.alpha.-(3-phenylpropyl)-[1,1'-biphenyl]-4-butanoic acid (86) was prepd. via alkylation of di-Et (3-phenylpropyl)malonate with 2,4'-dibromoacetophenone, followed by sapon.-monodecarboxylation, reaction with 4-methoxybenzeneboronic acid, Me ether cleavage, and O-pentylation. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. Using compds. such as 86, the no. of tumor metastases was decreased between 38 and 49% as compared to the control. The title compds. were also assayed for inhibition of cartilage lesions in a guinea pig model of osteoarthritis.

IT **179544-50-4P 179544-58-2P 179544-62-8P**
179546-96-4P 179547-63-8P
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

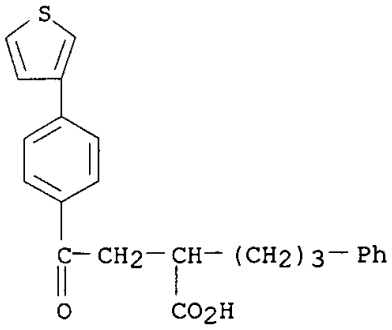
RN 179544-50-4 HCAPLUS

CN Benzenepentanoic acid, .alpha.-[2-[4-(5-chloro-2-thienyl)phenyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

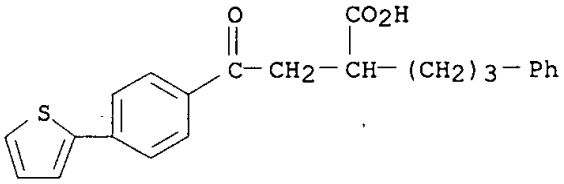


RN 179544-58-2 HCAPLUS

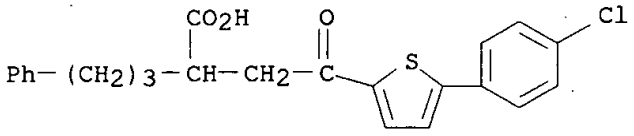
CN Benzenepentanoic acid, .alpha.-[2-oxo-2-[4-(3-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



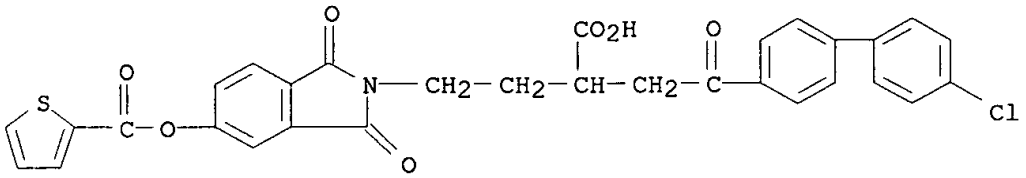
RN 179544-62-8 HCAPLUS
CN Benzenepentanoic acid, .alpha.-[2-oxo-2-[4-(2-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 179546-96-4 HCAPLUS
CN 2-Thiophenebutanoic acid, 5-(4-chlorophenyl)-.gamma.-oxo-.alpha.-(3-phenylpropyl)- (9CI) (CA INDEX NAME)

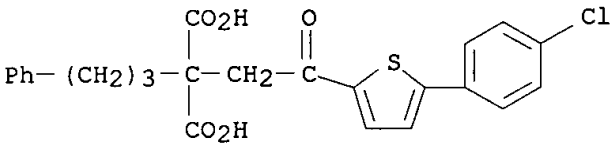


RN 179547-63-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-5-[(2-thienylcarbonyl)oxy]- (9CI) (CA INDEX NAME)



IT **179548-72-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of substituted biarylbutyric or biarylpentanoic acids and derivs. as matrix metalloprotease inhibitors)

RN 179548-72-2 HCAPLUS
CN Propanedioic acid, [2-[5-(4-chlorophenyl)-2-thienyl]-2-oxoethyl](3-phenylpropyl)- (9CI) (CA INDEX NAME)



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L10             STR
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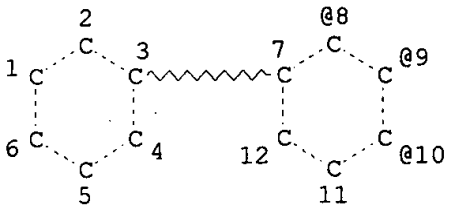

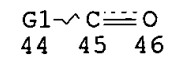


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  15

STEREO ATTRIBUTES: NONE
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                AS? OR METALLO(W)PROTEAS?)
L19          35 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 AND RESPIR?
L20           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L19
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L20 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:475626 HCAPLUS
DN 133:89429
TI Preparation of 4-aryl-4-oxo-2-(2-phthalimidoethyl)butanoates and analogs as matrix metalloprotease inhibitors
IN Fitzgerald, Mary F.; Gardiner, Philip J.; Nash, Kevin; Sturton, Graham; Benz, Gunter; Henning, Rolf; Schlemmer, Karl-Heinz; Riedl, Bernd; Haning, Helmut
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000040539	A1	20000713	WO 1999-EP10110	19991220
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1140768	A1	20011010	EP 1999-963582	19991220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9916669	A	20011016	BR 1999-16669	19991220
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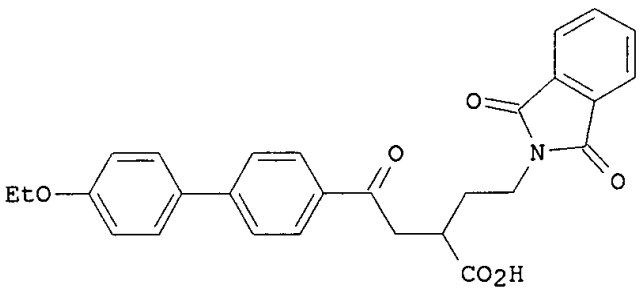
	GB 1999-22709	A	19990924		
	WO 1999-EP10110	W	19991220		

OS MARPAT 133:89429
GI



II

AB RZZ1Z2CO2H [I; R = (un)substituted Ph or -heteroaryl; Z = bond, (un)substituted 1,4-phenylene, -heteroarylene; Z1 = CO, CH(OH), C(:NOH), etc.; Z2 = substituted (CH2)2-3] were prepd. Thus, di-tert-Bu

PCT Equivalent -search Report attached

2-(2-phthalimidoethyl)malonate was condensed with 4-(EtO)C6H4C6H4(COCH2Br)-4 (prepn. each given) and the sapond. product mono-decarboxylated to give title compd. II. Data for biol. activity of I were given.

IT **179545-26-7P 179546-43-1P 179546-44-2P**
179546-45-3P 179546-46-4P 179546-47-5P
179547-07-0P 179547-30-9P 179547-31-0P
179547-32-1P 179547-35-4P 179547-36-5P
179547-37-6P 179547-42-3P 179547-43-4P
179547-44-5P 179547-45-6P 179547-48-9P
179547-53-6P 179547-54-7P 179547-55-8P
179547-56-9P 179547-58-1P 179547-59-2P
179547-60-5P 179547-61-6P 179547-62-7P
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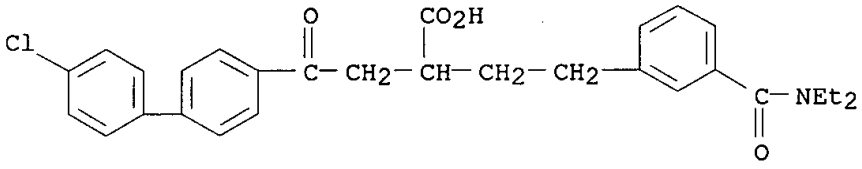
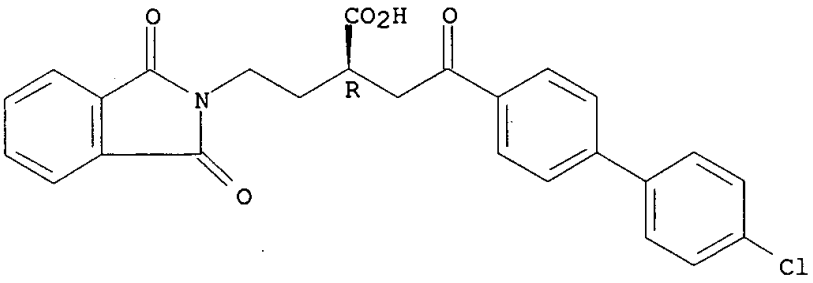
282095-29-8P 282095-31-2P 282095-34-5P
282095-36-7P 282095-38-9P 282095-40-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-aryl-4-oxo-2-(2-phthalimidoethyl)butanoates and analogs as **matrix metalloprotease** inhibitors)

RN 179545-26-7 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.alpha.-[2-[3-[(diethylamino)carbonyl]phenyl]ethyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)

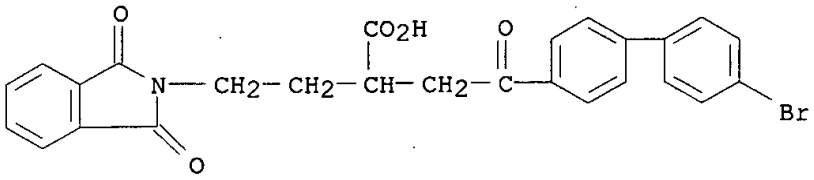


RN 179546-43-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 179546-44-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



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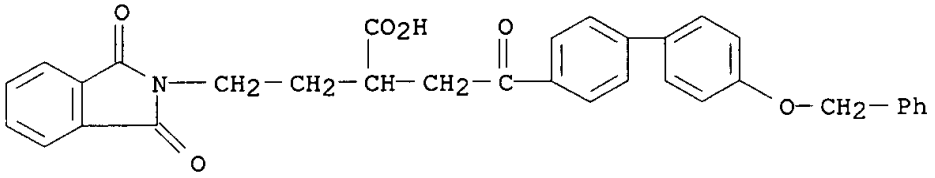
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-(phenylmethoxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)



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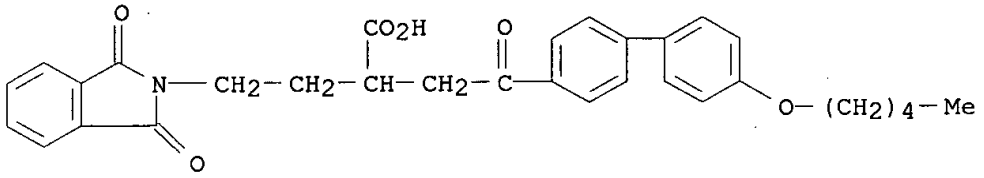
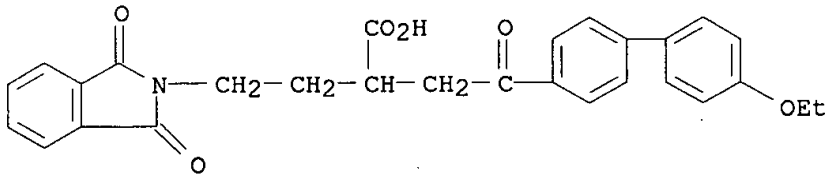
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-1,3-dioxo-.alpha.-[2-oxo-2-[4'-(pentyloxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)

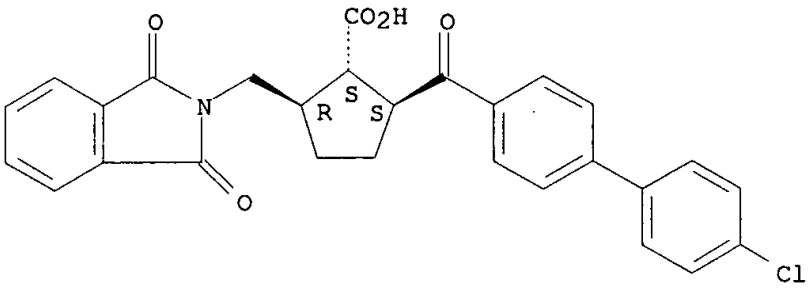


RN 179546-47-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



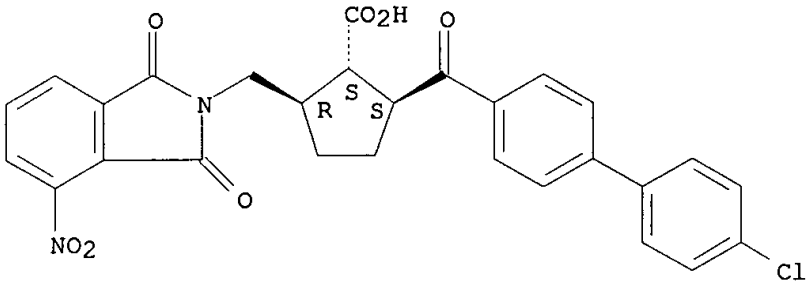
RN 179547-07-0 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



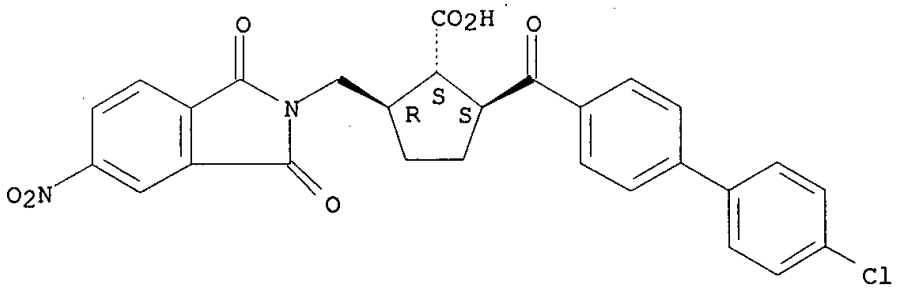
RN 179547-30-9 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-4-nitro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

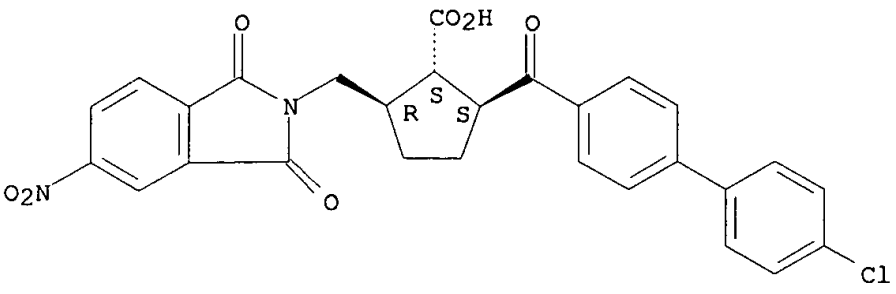
Relative stereochemistry.



RN 179547-31-0 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-5-nitro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

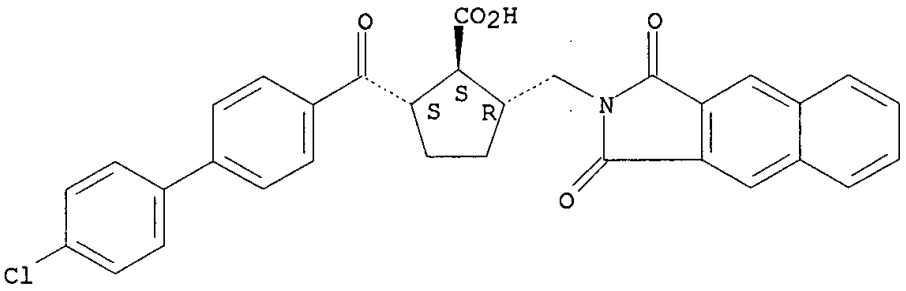
Relative stereochemistry.





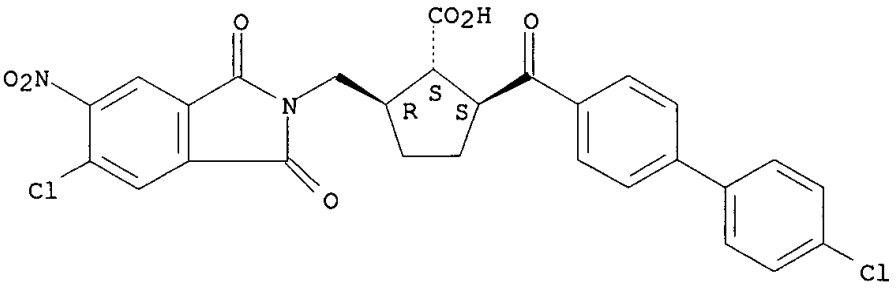
RN 179547-32-1 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



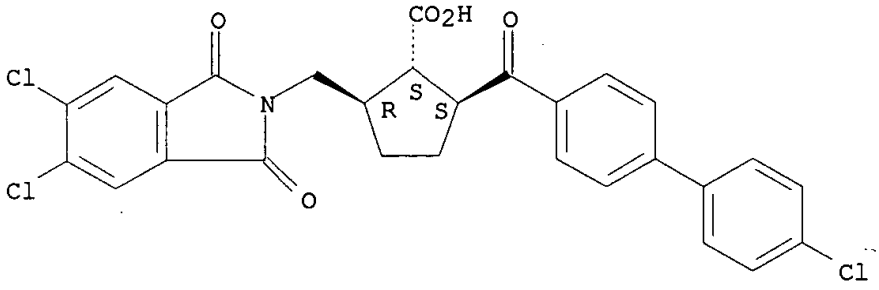
RN 179547-35-4 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(5-chloro-1,3-dihydro-6-nitro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



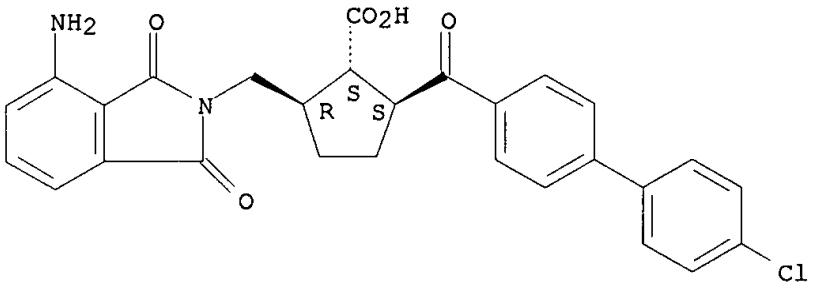
RN 179547-36-5 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(5,6-dichloro-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



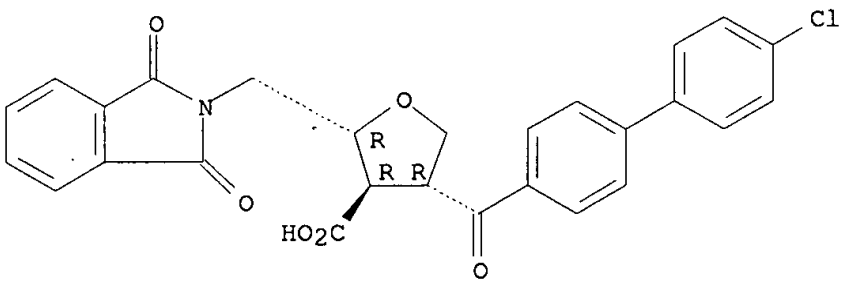
RN 179547-37-6 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4-amino-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-5-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-, (1R,2S,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



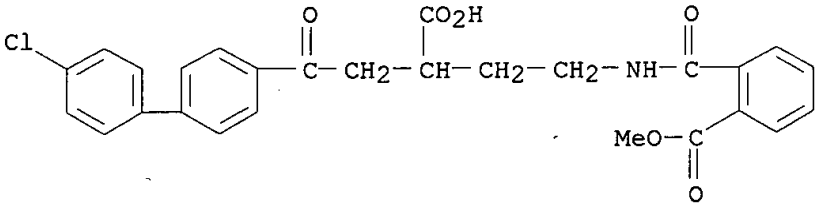
RN 179547-42-3 HCAPLUS
CN 3-Furancarboxylic acid, 4-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-2-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]tetrahydro-, (2R,3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

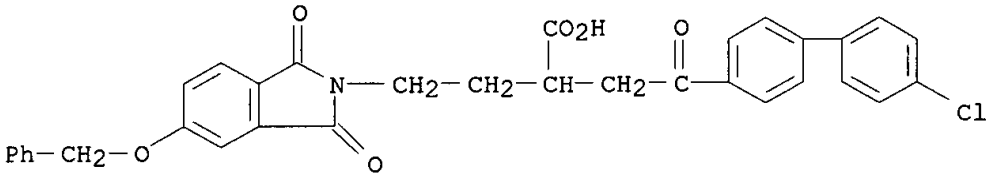


RN 179547-43-4 HCAPLUS

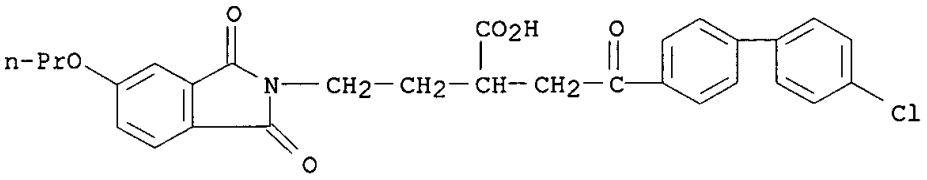
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.alpha.-[2-[[2-(methoxycarbonyl)benzoyl]amino]ethyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



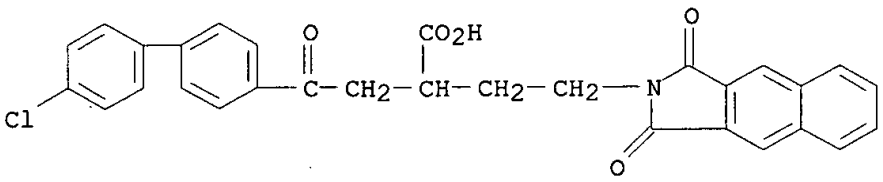
RN 179547-44-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 179547-45-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-5-propoxy- (9CI) (CA INDEX NAME)

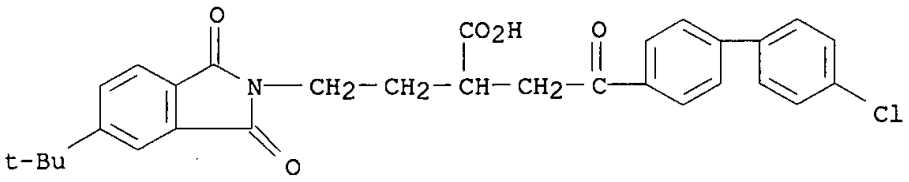


RN 179547-48-9 HCAPLUS
CN 2H-Benz[f]isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

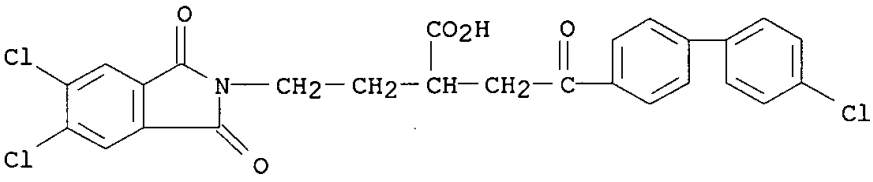


RN 179547-53-6 HCAPLUS

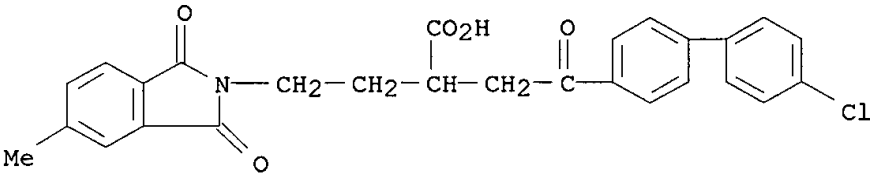
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-5-(1,1-dimethylethyl)-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



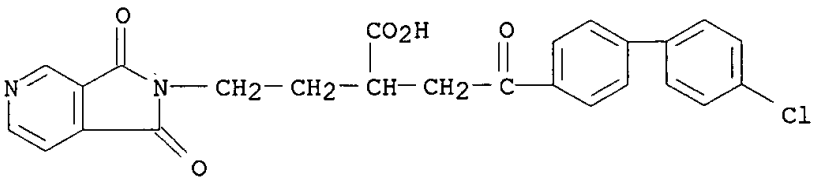
RN 179547-54-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 5,6-dichloro-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-55-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-5-methyl-1,3-dioxo- (9CI) (CA INDEX NAME)

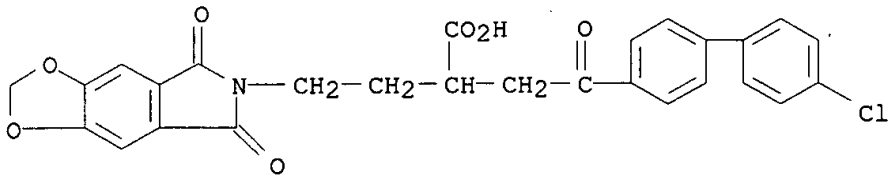


RN 179547-56-9 HCAPLUS
CN 2H-Pyrrolo[3,4-c]pyridine-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

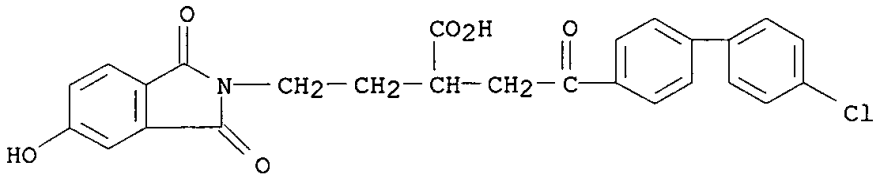


RN 179547-58-1 HCAPLUS

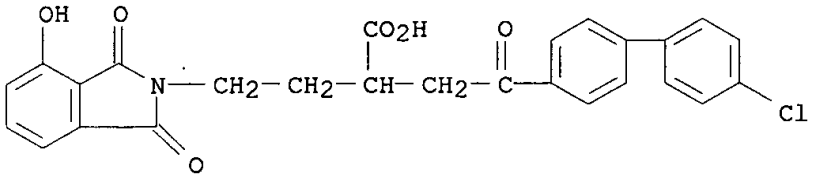
CN 6H-1,3-Dioxolo[4,5-f]isoindole-6-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-5,7-dihydro-5,7-dioxo- (9CI) (CA INDEX NAME)



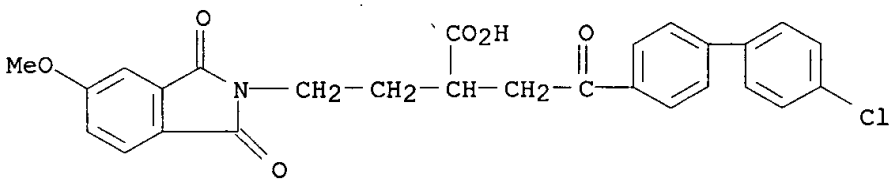
RN 179547-59-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-5-hydroxy-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 179547-60-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-4-hydroxy-1,3-dioxo- (9CI) (CA INDEX NAME)

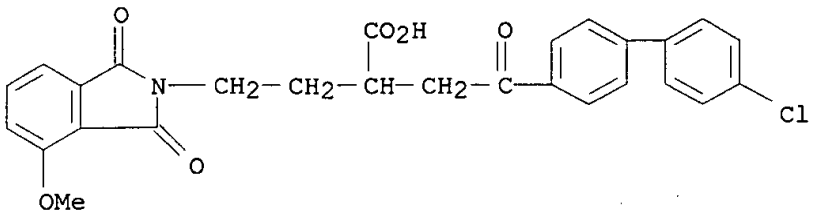


RN 179547-61-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-5-methoxy-1,3-dioxo- (9CI) (CA INDEX NAME)

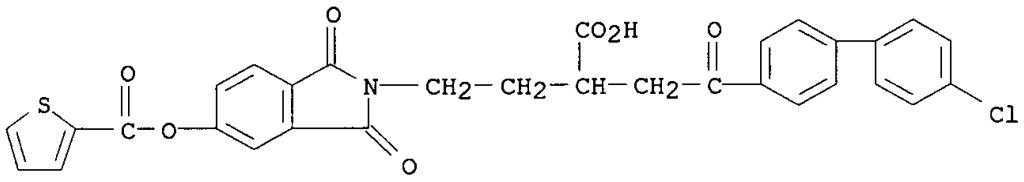


RN 179547-62-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-

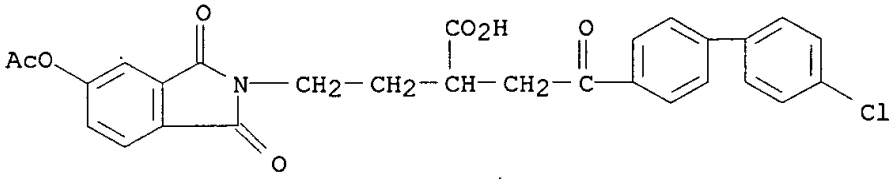
oxoethyl]-1,3-dihydro-4-methoxy-1,3-dioxo- (9CI) (CA INDEX NAME)



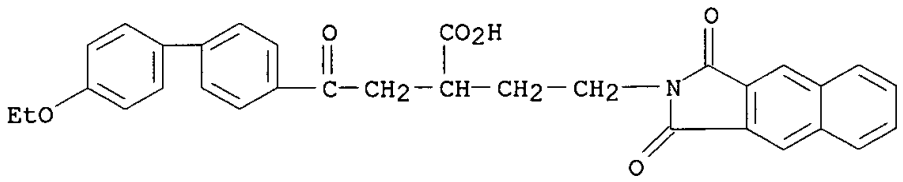
RN 179547-63-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-5-[(2-thienylcarbonyl)oxy]- (9CI) (CA INDEX NAME)



RN 179547-64-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 5-(acetyloxy)-.alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

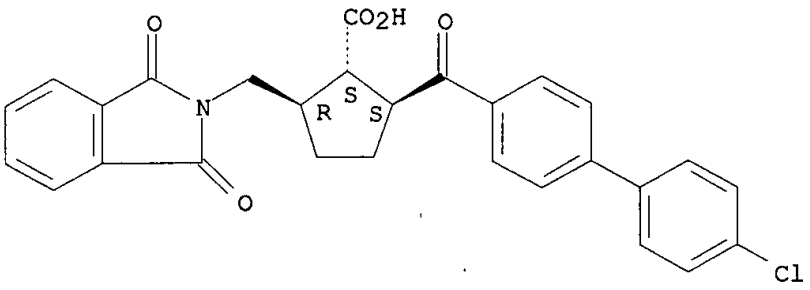


RN 179547-68-3 HCAPLUS
CN 2H-Benz[f]isoindole-2-butanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



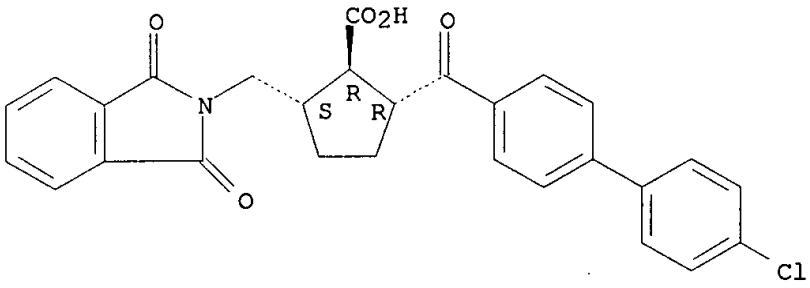
RN 179798-06-2 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1S,2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

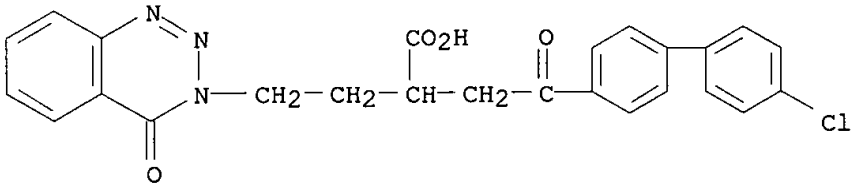


RN 179798-07-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, (1R,2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



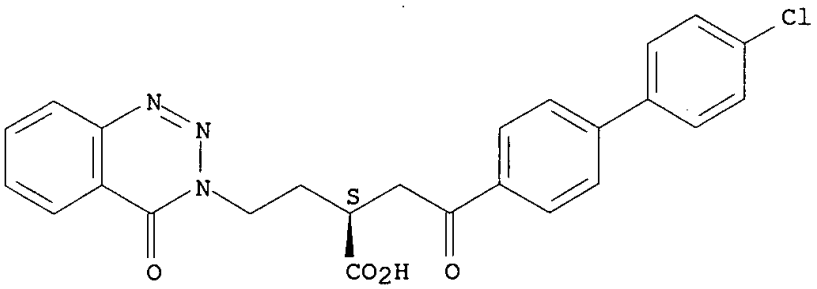
RN 199437-84-8 HCAPLUS
CN 1,2,3-Benzotriazine-3(4H)-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-4-oxo- (9CI) (CA INDEX NAME)



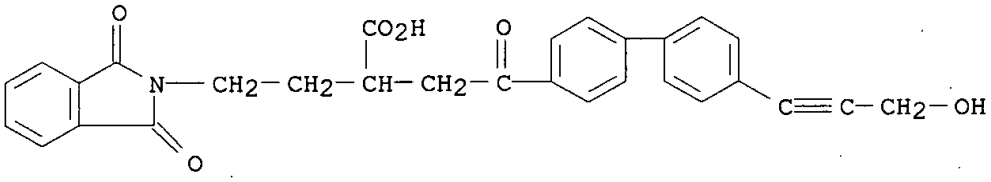
RN 199437-86-0 HCAPLUS
CN 1,2,3-Benzotriazine-3(4H)-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-

biphenyl]-4-yl)-2-oxoethyl]-4-oxo-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

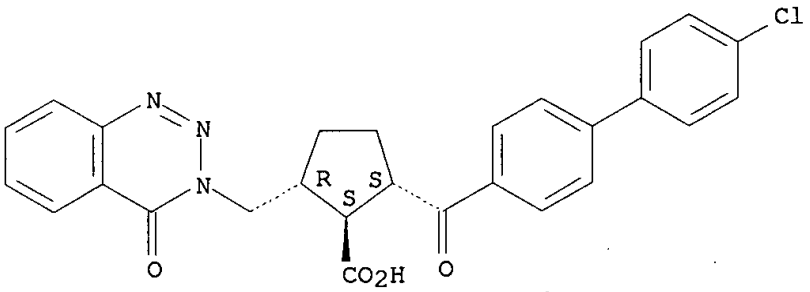


RN 199672-21-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-.alpha.-[2-[4'-(3-hydroxy-1-propynyl)[1,1'-biphenyl]-4-yl]-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)



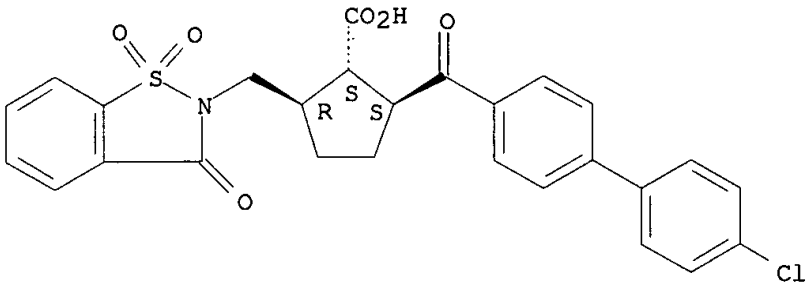
RN 230959-73-6 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



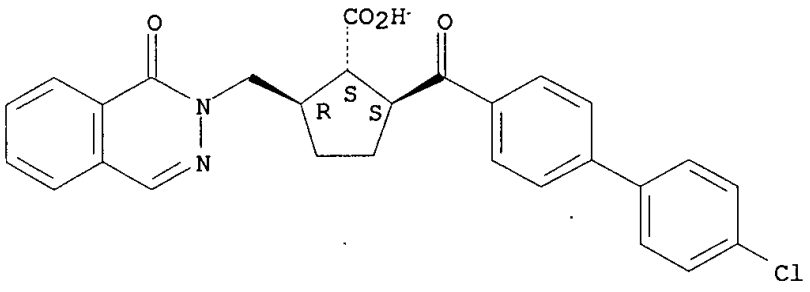
RN 230959-76-9 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



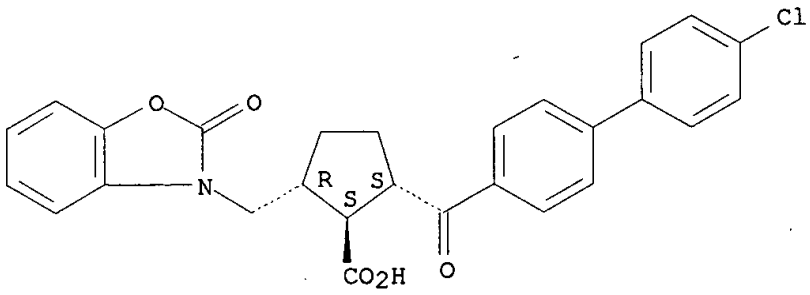
RN 230959-77-0 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(1-oxo-2(1H)-phthalazinyl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 230959-78-1 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-[(2-oxo-3(2H)-benzoxazolyl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

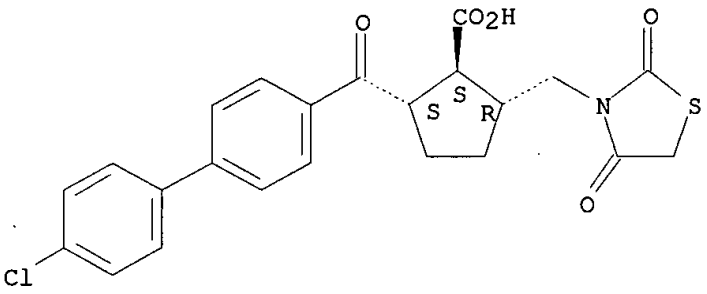
Relative stereochemistry.



RN 230959-80-5 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)carbonyl]-5-

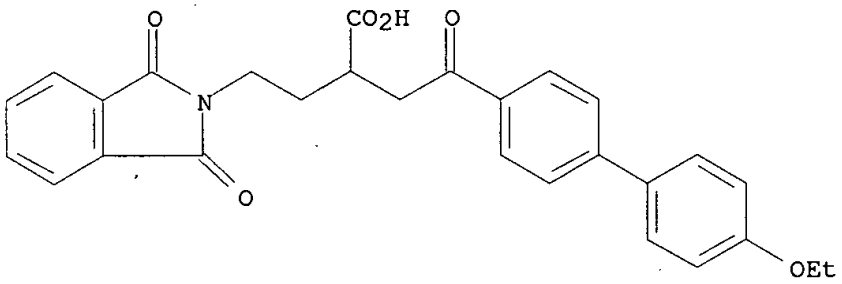
[(2,4-dioxo-3-thiazolidinyl)methyl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



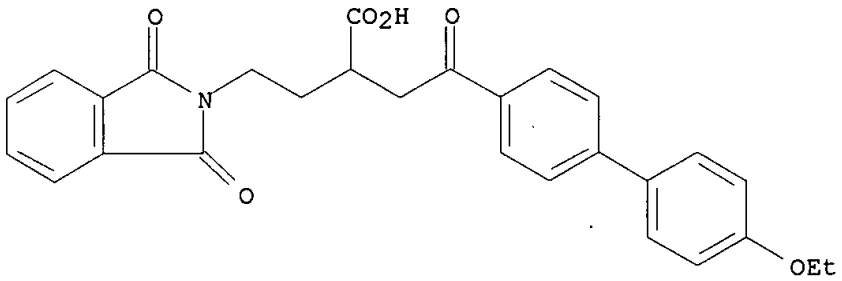
RN 282095-17-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



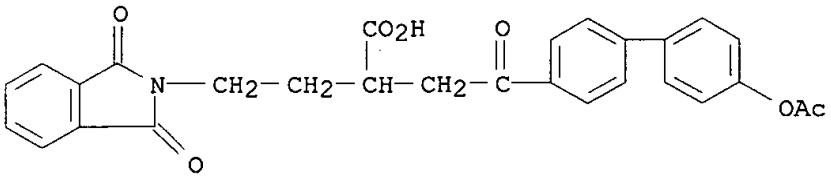
RN 282095-19-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

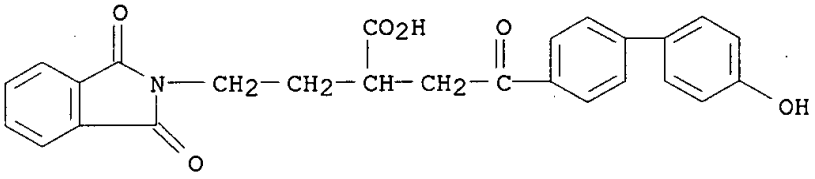


RN 282095-22-1 HCAPLUS

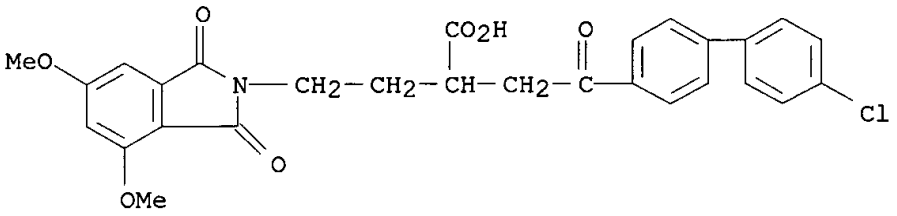
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-[4'-(acetyloxy)[1,1'-biphenyl]-4-yl]-2-oxoethyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 282095-24-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-.alpha.-[2-(4'-hydroxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)

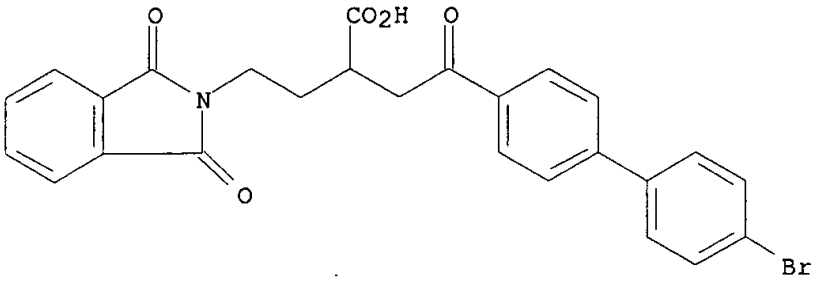


RN 282095-26-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-4,6-dimethoxy-1,3-dioxo- (9CI) (CA INDEX NAME)



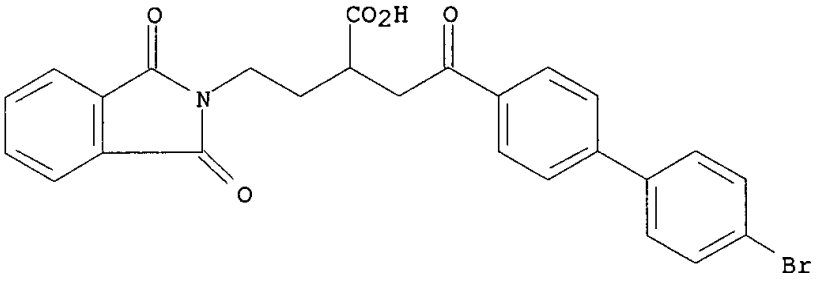
RN 282095-29-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



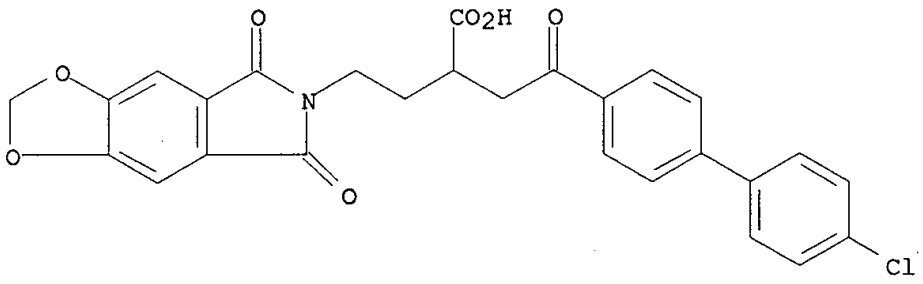
RN 282095-31-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[2-(4'-bromo[1,1'-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



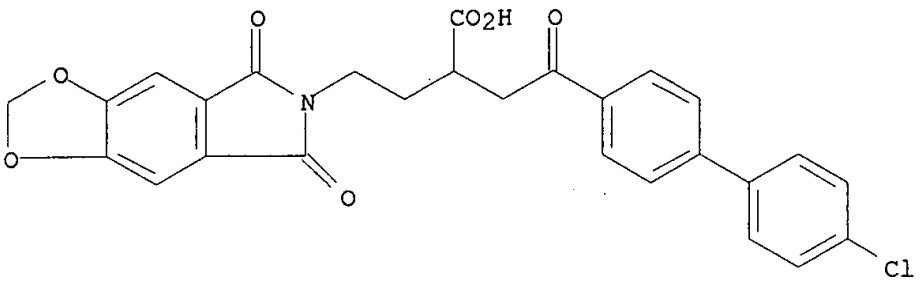
RN 282095-34-5 HCAPLUS
CN 6H-1,3-Dioxolo[4,5-f]isoindole-6-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-5,7-dihydro-5,7-dioxo-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

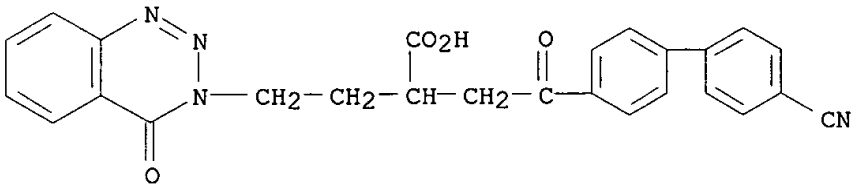


RN 282095-36-7 HCAPLUS
CN 6H-1,3-Dioxolo[4,5-f]isoindole-6-butanoic acid, .alpha.-[2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl]-5,7-dihydro-5,7-dioxo-, (-)- (9CI) (CA INDEX NAME)

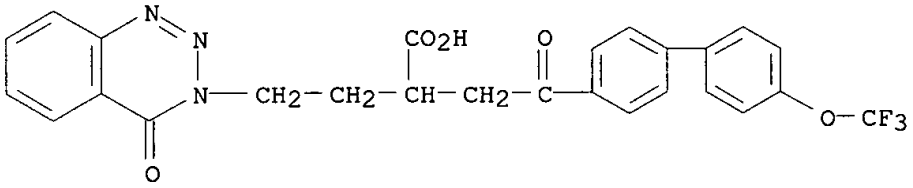
Rotation (-).



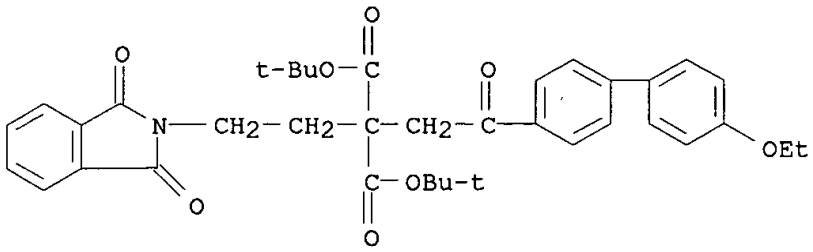
RN 282095-38-9 HCAPLUS
CN 1,2,3-Benzotriazine-3(4H)-butanoic acid, .alpha.-[2-(4'-cyano[1,1'-biphenyl]-4-yl)-2-oxoethyl]-4-oxo- (9CI) (CA INDEX NAME)



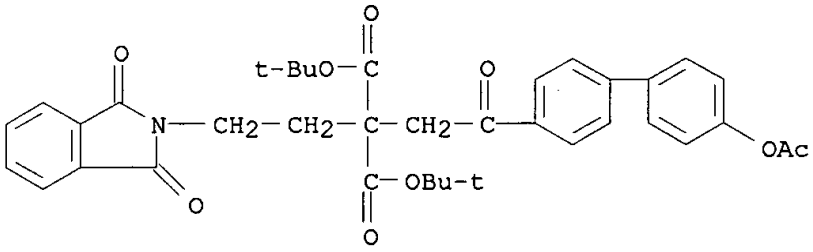
RN 282095-40-3 HCAPLUS
CN 1,2,3-Benzotriazine-3(4H)-butanoic acid, 4-oxo-.alpha.-[2-oxo-2-[4'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)



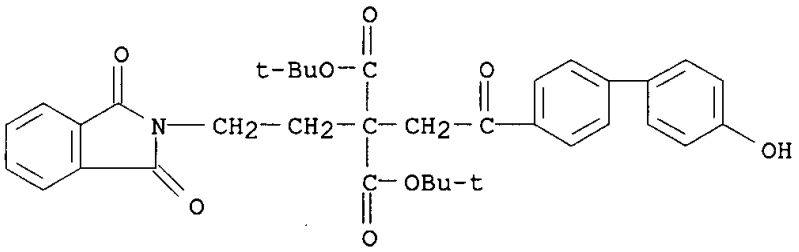
IT **282095-67-4P 282095-69-6P 282095-70-9P**
282095-72-1P 282095-73-2P 282095-76-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 4-aryl-4-oxo-2-(2-phthalimidoethyl)butanoates and analogs as **matrix metalloprotease** inhibitors)
RN 282095-67-4 HCAPLUS
CN Propanedioic acid, [2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl][2-(4'-ethoxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



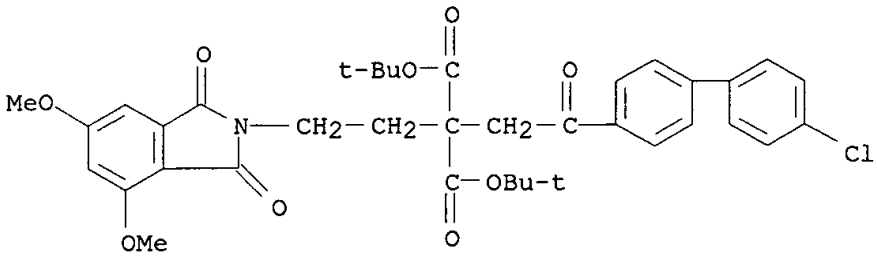
RN 282095-69-6 HCAPLUS
CN Propanedioic acid, [2-[4'-(acetyloxy)[1,1'-biphenyl]-4-yl]-2-oxoethyl][2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



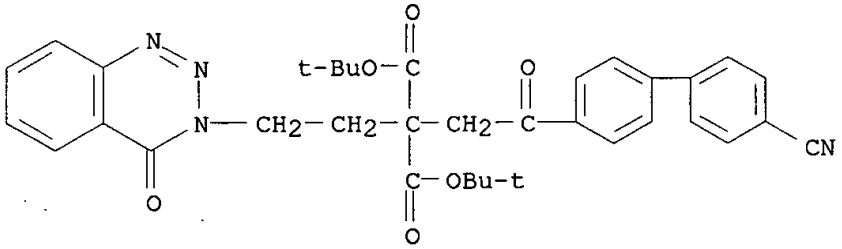
RN 282095-70-9 HCAPLUS
CN Propanedioic acid, [2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl][2-(4'-hydroxy[1,1'-biphenyl]-4-yl)-2-oxoethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



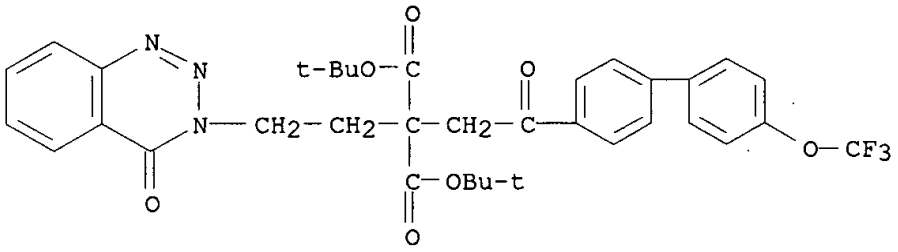
RN 282095-72-1 HCAPLUS
CN Propanedioic acid, [2-(4'-chloro[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(1,3-dihydro-4,6-dimethoxy-1,3-dioxo-2H-isoindol-2-yl)ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 282095-73-2 HCAPLUS
CN Propanedioic acid, [2-(4'-cyano[1,1'-biphenyl]-4-yl)-2-oxoethyl][2-(4-oxo-1,2,3-benzotriazin-3(4H)-yl)ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 282095-76-5 HCAPLUS
CN Propanedioic acid, [2-(4-oxo-1,2,3-benzotriazin-3(4H)-yl)ethyl][2-oxo-2-[4'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]ethyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

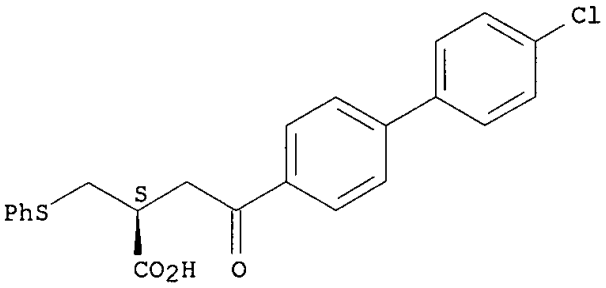
L20 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:764013 HCAPLUS
DN 132:12201
TI Preparation of biarylalkylhydroxamic acids and related compounds as matrix metalloprotease inhibitors.
IN Kluender, Harold C. E.; Brittelli, David R.; Schoen, William R.; Ha,

Sookhee N.
PA Bayer Corporation, USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9961413	A1	19991202	WO 1999-US11481	19990525
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6288063	B1	20010911	US 1998-85909	19980527
AU 9942017	A1	19991213	AU 1999-42017	19990525
EP 1082295	A1	20010314	EP 1999-925802	19990525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1998-85909 A 19980527
WO 1999-US11481 W 19990525
OS MARPAT 132:12201
AB TxABDEG [A = Ph, thienyl, furyl, pyrrolyl, oxazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, etc.; B = bond, thienylene, furylene, phenylene, furylene, imidazolylene, pyridinylene, pyrazinylene, pyridazinylene, etc.; T = halo, alkyl, haloalkyl, haloalkoxy, alkenyl, alkynyl, etc.; x = 0, 1, 2; D = CO, CH(OH), C:NN(R2)2, C:NOR2; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; E = 2-3 C atom chain bearing 1-3 substituents; G = COCH2OH, CONHOH, CONHSO2R3; R3 = alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl], were prepd. as matrix metalloproteinase inhibitors (no data). Thus, 4-(biphen-4-yl)-4-oxobutyric acid in EtOAc/CH2Cl2 was treated with CH2N2 in Et2O to give 100% Me ester, which was added to a soln. of NH2OH.HCl and KOH in MeOH/H2O to give 4-Ph6H4C(:NOH)CH2CH2CONOH.
IT **179545-77-8**
RL: RCT (Reactant)
(prepn. of biarylalkylhydroxamic acids and related compds. as **matrix metalloprotease** inhibitors)
RN 179545-77-8 HCAPLUS
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-[(phenylthio)methyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT